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JUNE 1958

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THE American JOURNAL OF Surgery

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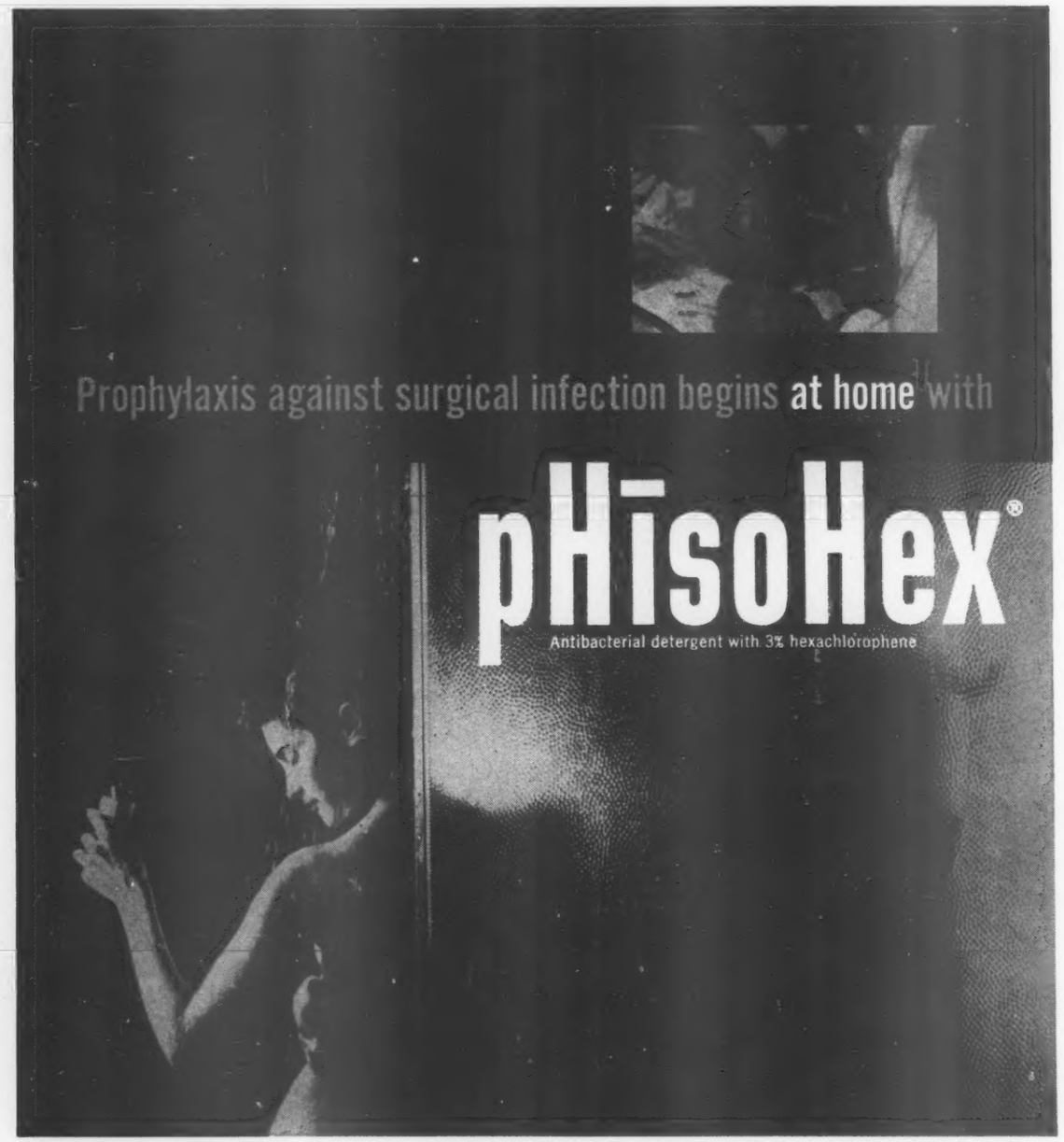
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CHARLES S. TANNENBAUM

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PAUL J. CONNOLLY, WILLIAM S. CARPENTER AND CHARLES G. JOHNSTON

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1. *Rushia, E. L.: Preliminary report on the use of meprobamate for pre-anesthetic sedation. J.M.A. Georgia* **46**:*93, March 1957.*
2. *Lamphier, T. A.: The role of meprobamate in postoperative surgical care. Ann. New York Acad. Sc.* **67**:*810, May 9, 1957.*
3. *Kern, E. C.: Preoperative sedation with meprobamate (Miltown) in surgery of eye, ear, nose and throat. Eye, Ear, Nose & Throat Month.* **36**: *408, July 1957.*

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F. PAUL ANSBRO, ALBERT E. BLUNDELL, WILBERT E. HERNANDEZ AND JAMES V. CARTER

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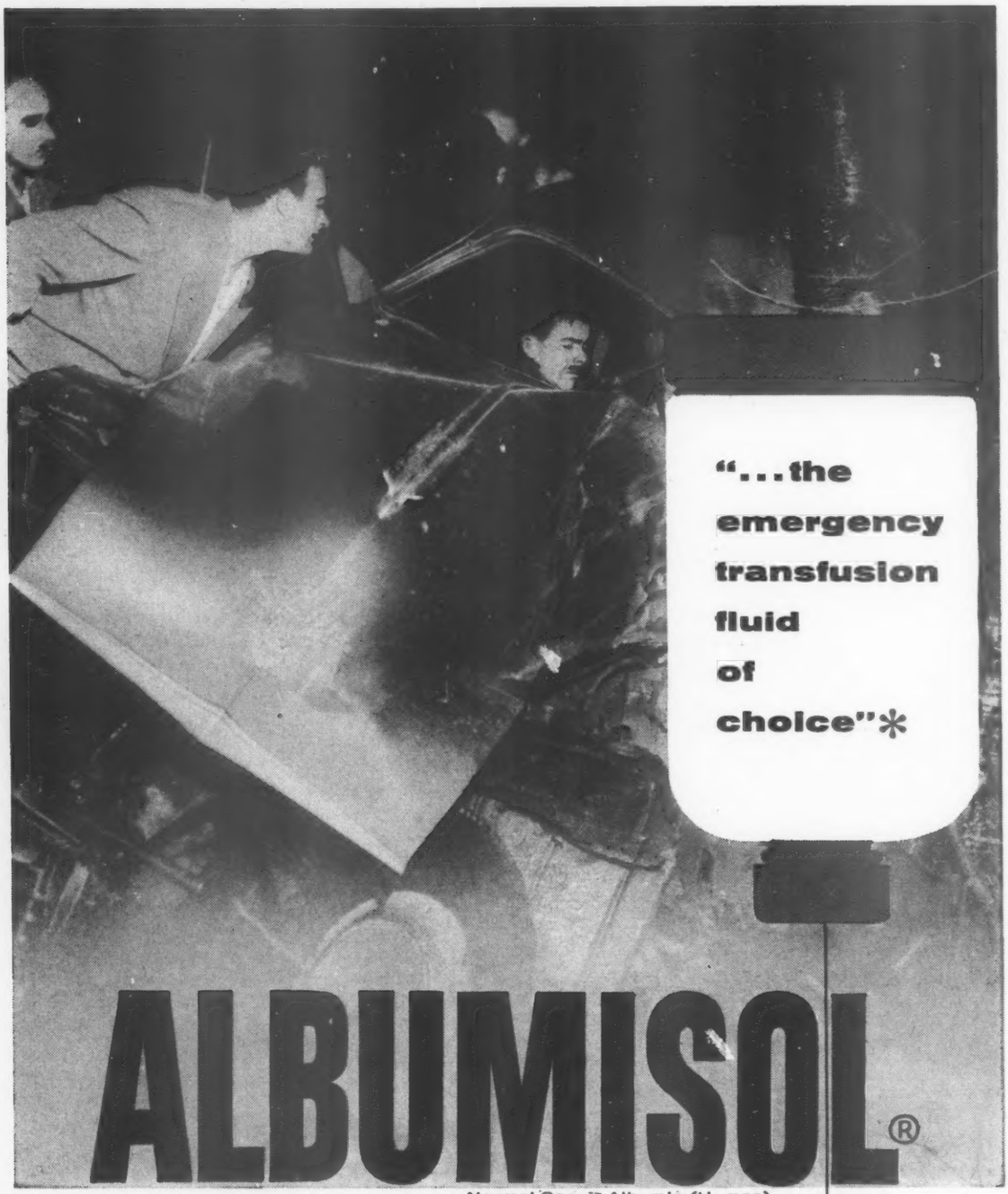

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IRVING ROSENBERG AND SOL ROSEN

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Cholecystitis in a Four Year Old Child 1013

FRANK E. BARNES, JR.

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Sacrococcygeal Teratoma 1015

GILMAN DEERING KIRK

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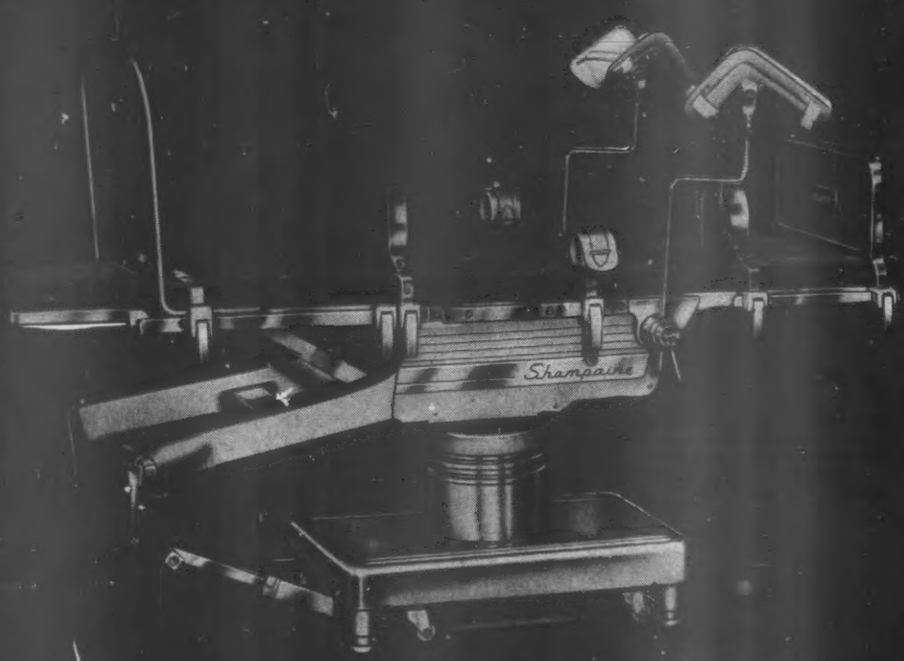

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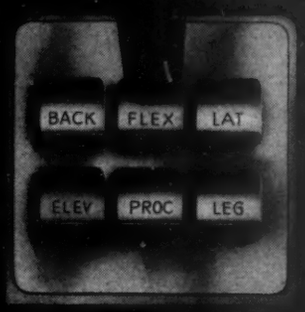

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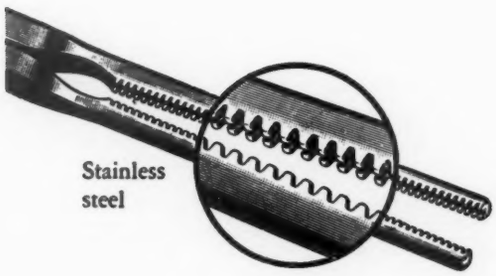

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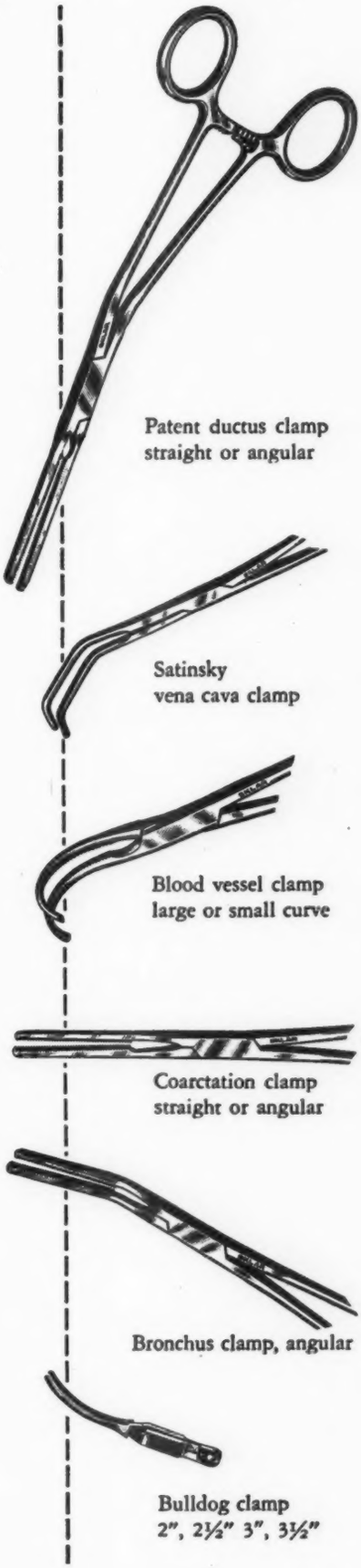

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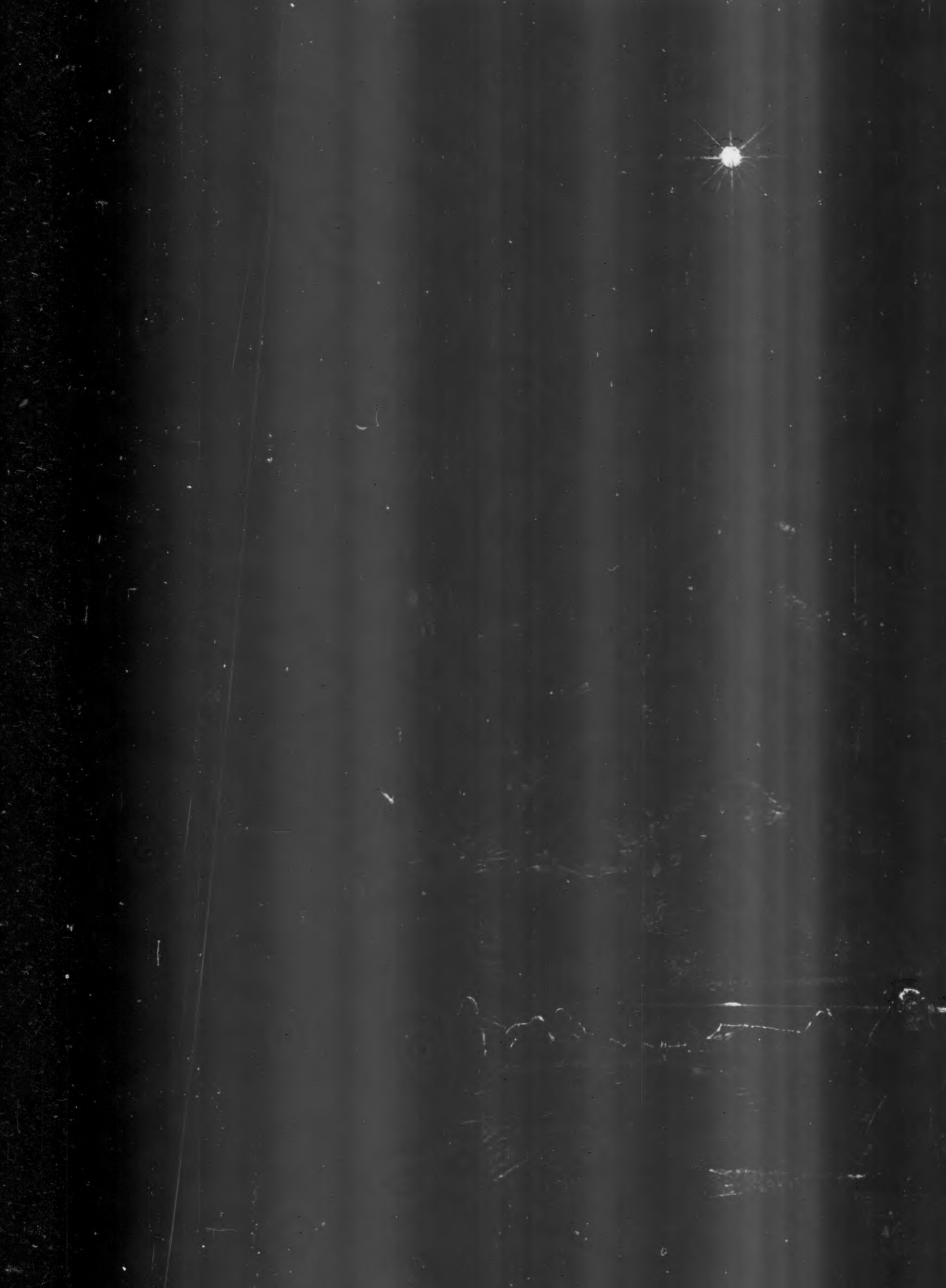

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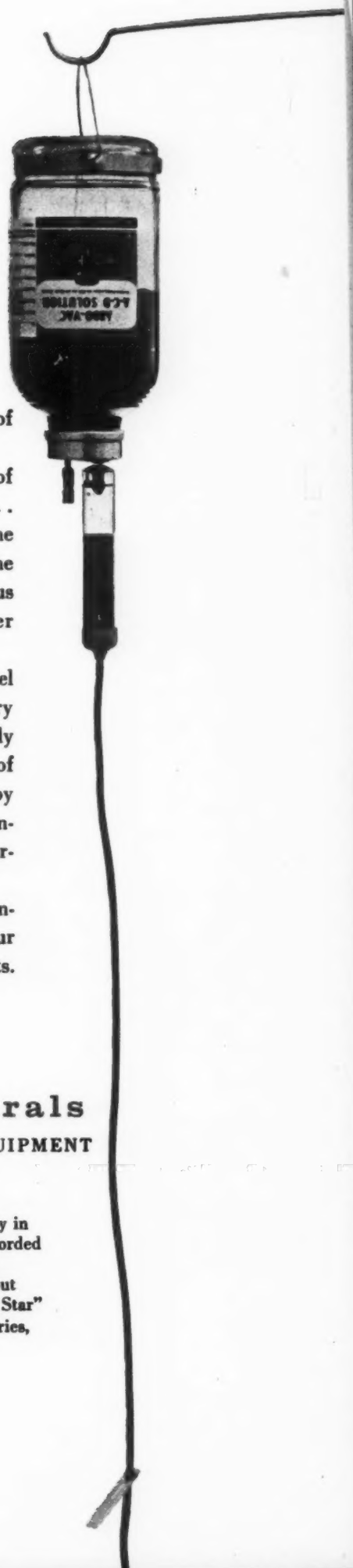

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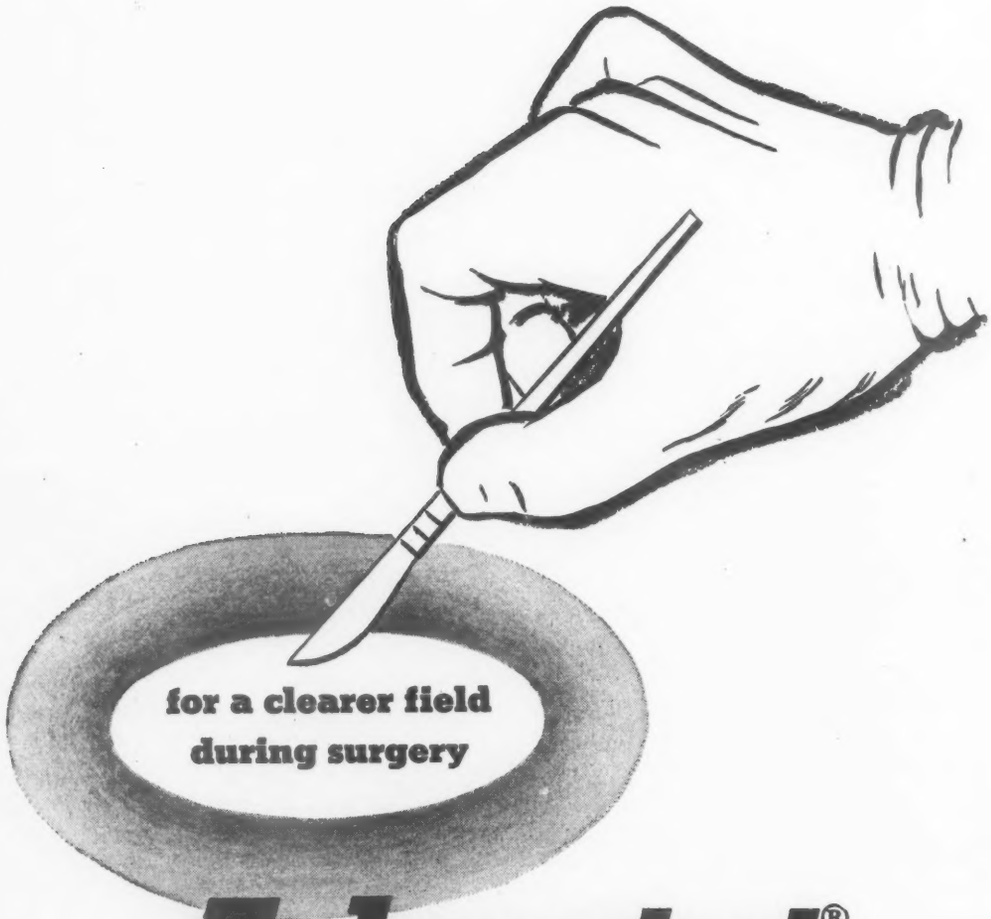

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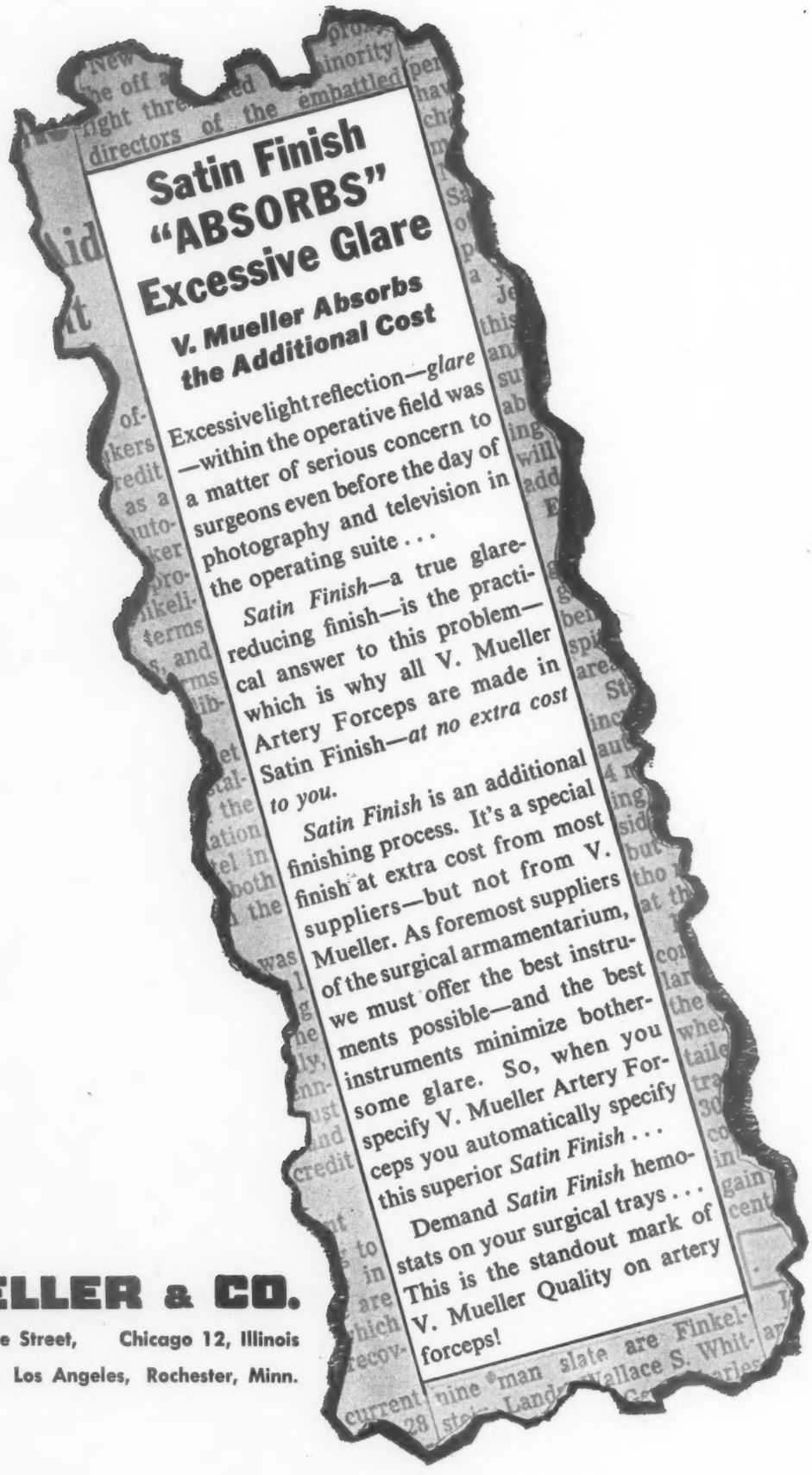

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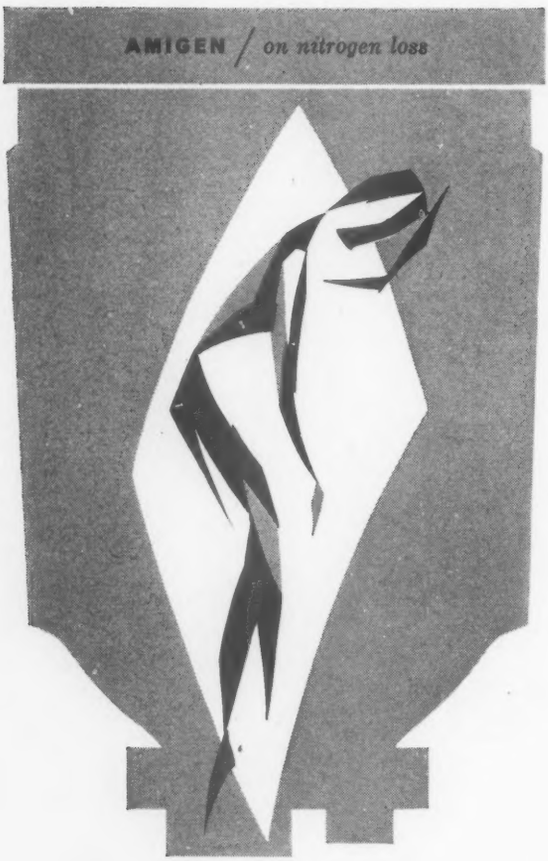

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1. Holden, W. D.; Krieger, H.; Levey, S., and Abbott, W. E.: Ann. Surg. 146:563 (Oct.) 1957.
2. Elman, R.: J. Am. Dietet. Assoc. 32:521 (June) 1956.

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1. Helms, W. C.: J. M. A. Georgia 42:376, 1953. 2. Rogers, S. P., and Moore, J.: Texas J. M. 53:338, 1957. 3. Schwartz, J.: Am. J. Obst. 63:579, 1952.

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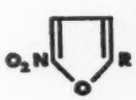

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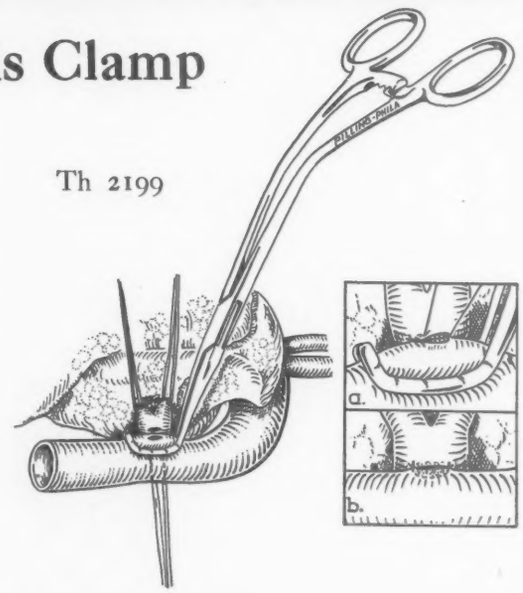

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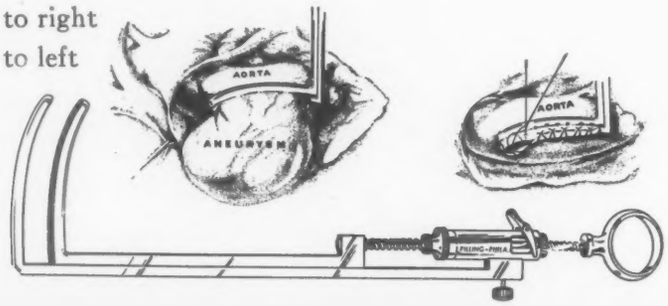

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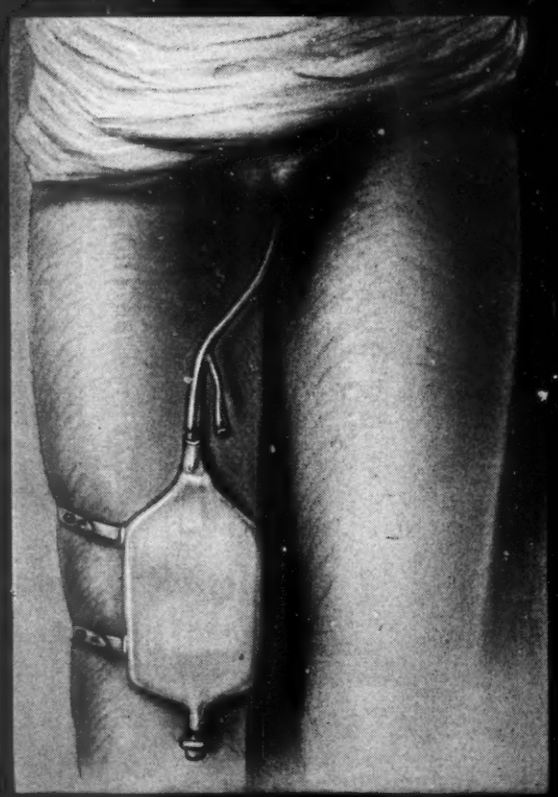

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* Jackson, A. S.: Journal-Lancet *76*:45 (Feb.) 1956.

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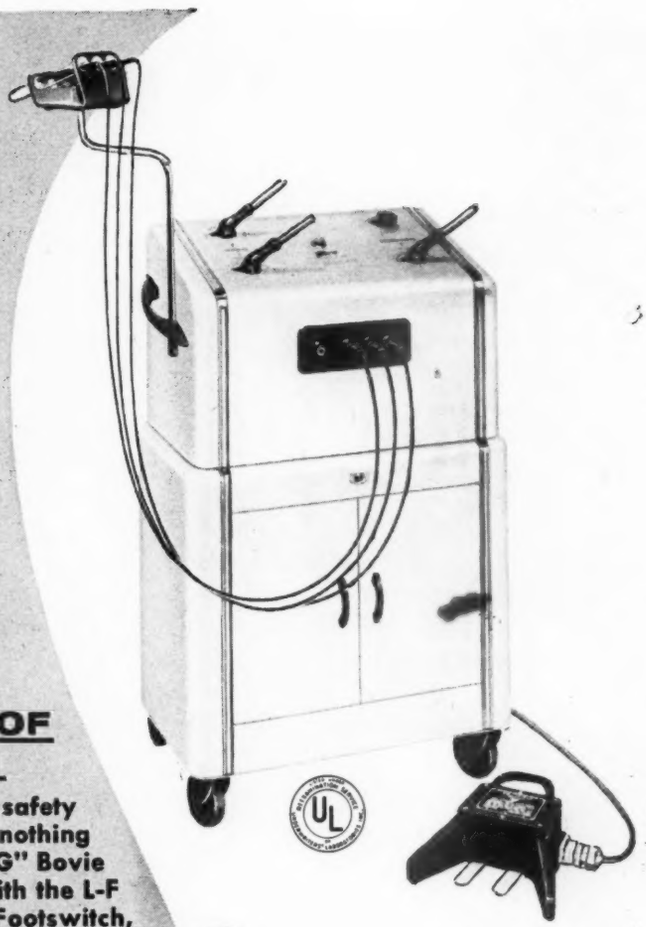

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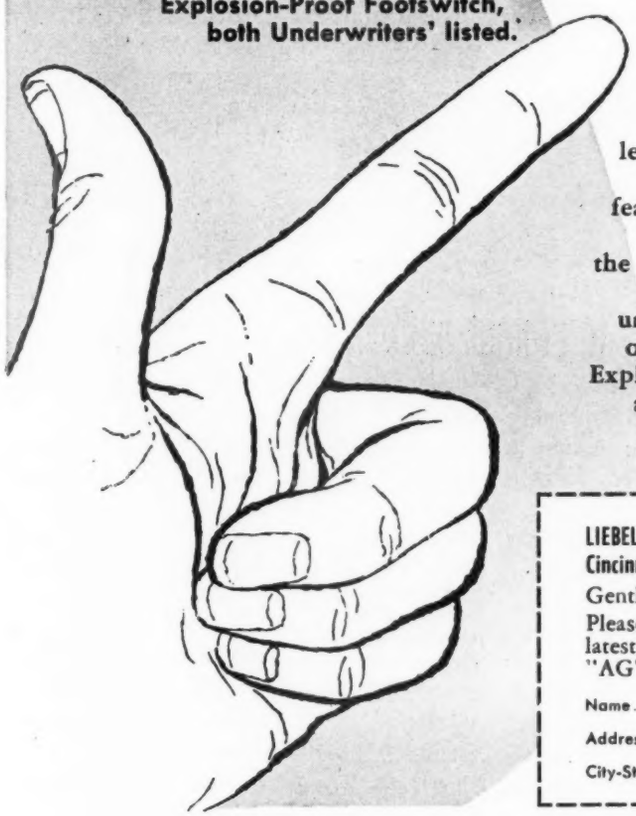

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The American Journal of Surgery

VOLUME 95 JUNE 1958 NUMBER SIX

EDITORIAL

Autogenous Skin Bank

THE split-thickness graft is highly useful in many situations encountered in the field of general surgery. Actually its usefulness seems to be increasing as the scope of surgery widens. In addition to the time-honored use of grafts in burns of the body we are seeing more and more applications of grafting procedures after highway and industrial accidents in which skin and soft tissues have been lost. Also, radical resections for malignant disease commonly leave large defects in body surface requiring coverage by skin. As examples of this we have the radical mastectomy, surgery of the head and neck, and resections of malignant soft tissue tumors.

The new electrodermatomes and improved models of glue-type dermatomes have greatly simplified the removal of split-thickness grafts and have thus encouraged increased use of grafting procedures by general surgeons. The more complicated forms of skin transfers, such as tube grafts and delayed grafts, are properly left to the specialist in plastic surgery; however, the application of the simple Thiersch graft to provide surface covering after injury or surgery is well within the province of the general surgeon.

The skin graft as applied by the general surgeon is, by and large, a utilitarian procedure. Its purpose is to cover a surface defect as quickly as possible so as to promote healing, to prevent infection, to reduce morbidity and, at times, to save life by halting the progressive debility due to the effects of large denuded surfaces. In these situations the cosmetic result is of secondary importance.

For these reasons the general surgeon often finds it advisable to apply grafts under somewhat less than ideal conditions. For example, in a badly burned patient it is not always possible to wait for the recipient area to appear perfectly clean and healthy before grafting is started. Likewise, after radical resections for tumor the area to be grafted may offer difficult contours and positions and be subject to almost constant contamination. Nevertheless, in the interest of obtaining a healed wound as quickly as possible the surgeon must apply the skin graft under these adverse conditions. Such skin grafts do not always result in a 100 per cent "take," and second and third "sittings" are often necessary to obtain complete coverage.

For this reason, during the past two years we have set up an autogenous skin bank for most of our cases requiring skin grafts. Such banking of skin is simple to carry out, requires no special equipment and yet provides a ready supply of skin to "patch up" areas where skin has been lost from the original graft.

At the original operation enough skin is removed from the donor site to cover the defect; then, as the house officers say, "we take one more for the bank." This extra skin, together with small pieces left over after trimming the graft, is spread out on gauze soaked in a solution of some antibiotic (at present we are using a mixture of sulfamylon® and streptomycin) and stored in buffered saline solution at ordinary refrigerator temperatures in covered but unsealed containers. This simple method of storing skin seems to work well in autografts. Considerable investigation has been carried out by various workers trying to find

the best method of preserving and storing skin. Such methods include special nutrient media, storage at low temperatures, ultrarapid cooling (vitrification) and lyophilization. Many of these methods, however, are designed for mass preservation of homografts, usually grafts from cadavers. For our purposes, simple refrigeration in an antibiotic environment seems adequate.

This banked skin can be applied as necessary at a later date to cover areas in which the original graft has failed. We have used such stored skin successfully after three and four weeks of refrigeration. At times we have even applied patch grafts in the patient's own room without taking him to the operating suite. In such cases the grafts are held in place by nonadherent pressure dressings without sutures. The thickness of the stored grafts has varied widely. In secondary grafting of burns and mastectomy wounds, thin split-thickness skin has been used. In one case stored full-thickness skin was used successfully after a radical operation for surgical elephantiasis of the arm.

This plan offers several important advantages to the surgeon and his patient: (1) the patient can often be spared a second anesthetic since previously removed skin can be applied without anesthesia; (2) the patient is spared the additional expense of a second trip to the operating room; and (3) since the surgeon had readily available donor skin, he is more apt to graft small residual uncovered areas, thereby reducing morbidity and time spent by the patient in the hospital. Since the majority of grafts take without extensive loss, the unused grafts tend to accumulate, and at times the supply of skin in the bank can function as an emergency homograft source for burns and other traumatic emergencies. This added value justifies the routine banking of skin during grafting procedures, particularly in those hospitals with active emergency services.

To illustrate the effectiveness of this plan, we cite the case of a sixty-seven year old white woman who underwent radical mastectomy for carcinoma. It was possible to close the incision without grafting; however, one week following surgery wound infection developed and it was necessary to open the incision widely to establish free drainage. The infection subsided promptly, but in the process there was marked retraction of the skin flaps leaving a large skin defect on the chest wall. As soon as the gross infection had subsided, but before ideal conditions for grafting existed, the patient was taken to the operating room and the entire bare area was covered with split-thickness grafts. Extra skin was taken and preserved as described heretofore. When the dressings were removed some five days later, it was found that only about 70 per cent of the graft had taken. Therefore after treating the area with saline compresses for several days, the granulating areas were covered with stored skin. Again approximately 70 per cent of the grafts took, so the whole process was repeated. At the last sitting the skin had been refrigerated for three weeks. These final grafts took just as readily as fresh skin. The patient has been followed up for a little more than two years, and the grafted area has stood up well.

JOHN R. STEEPER, M.D. AND
VAUGHN DEMERGIAN, M.D.,
Department of Surgery, Jackson Clinic, Madison, Wisconsin

The Surgical Anatomy and Technic of Parotidectomy

OLIVER H. BEAHRS, M.D. AND MARTIN A. ADSON, M.D., *Rochester, Minnesota*

From the Section of Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

MORE than thirty years ago a few surgeons described and employed satisfactory surgical technics for the management of tumors of the parotid gland. However, the observation basic to these technics, namely that the facial nerve lay in a dissectable cleavage plane within the gland, at first was ignored and then was contested for many years. The relative rarity and varied pathologic types of parotid tumors brought confusion to pathologists and clinicians, whereas the occurrence of tumors in an unfamiliar vascular region penetrated by filaments of the nerve of facial expression fostered timidity in surgeons. As a result, general acceptance and modification of the basic procedures came about slowly.

Gradually, knowledge of the clinical behavior of parotid tumors has been accumulated, the results of haphazard operative procedures have been assessed and details of regional anatomy have been elucidated. At this higher level of understanding the indications for surgical intervention are more clear and several refinements of the original technics for parotidectomy are used commonly.

The busy surgeon, aware of the mass of literature contributing to this evolution, might question the need for another article on this subject. We do not depreciate the value of the existing literature; however, most surgical reports have lacked specific stepwise descriptions of technic and detailed anatomic information. Conversely, authors reporting comprehensive anatomic studies understandably have avoided the simplification and practical presentation looked for by the surgeon.

Results of ill planned operations in the parotid region are seen frequently because many surgeons, although competent in other fields, have little opportunity to acquire confidence in this location, where lesions are relatively uncommon. To this extent, a didactic description of anatomy and surgical technic appears justified. We have avoided formal review of the literature and discussion of clinicopathologic factors in the interest of brevity.

The following description of regional anatomy includes only those details of structure and variation having surgical significance. It is knowledge of the spatial relations of structures adjacent to and traversing the gland that is of primary importance to the surgeon undertaking parotidectomy. Detailed knowledge of the variable patterns of branching of the facial nerve and parotid duct has little practical application in surgical treatment of the parotid gland. This is particularly true if the trunk of the seventh nerve is identified as an initial step in the procedure.

SURGICAL ANATOMY

Skeletal Structures and Muscles. The parotid gland lies in and superficially overlaps the borders of a musculoskeletal recess formed by portions of the temporal bone, atlas and mandible, and their related muscles. The bony fossa is limited posteriorly by the anterior surface of the mastoid process. (Fig. 1.) Its

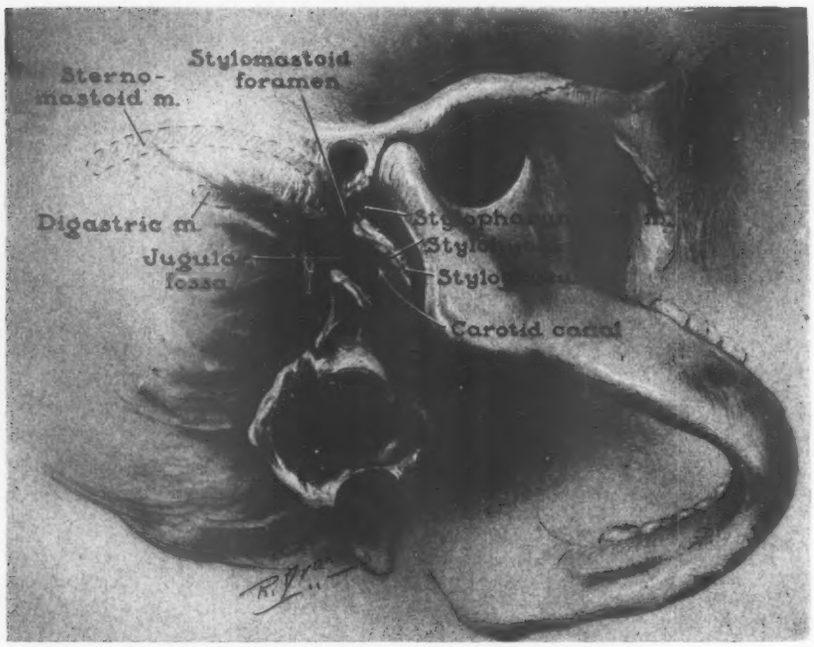

FIG. 1. The skeletal bed of the parotid gland.

superior margin is formed posterosuperiorly by the convex surface of the external acoustic meatus (cartilaginous portion superficially and osseous portion more deeply) and anterosuperiorly by the head of the mandible articulating in the mandibular fossa. Limited anteriorly by the ramus of the mandible, the skeletal framework is incomplete deep to that structure. Marking the medial wall of the bony recess superiorly is the styloid process with its sheath and, lower down, the surprisingly prominent tip of the transverse process of the atlas. This portion of the atlas can be palpated in a thin person roughly midway between the tip of the mastoid process and the angle of the mandible.

The positions of the carotid canal, jugular fossa and stylomastoid foramen as related to the base of the styloid process may be noted in Figure 1. The posterior root of origin of the zygomatic process of the temporal bone forms the posterior margin of the mandibular fossa; this portion of the process is closely related to the deep portion of the parotid gland. The rest of the zygomatic process bears a less intimate relation to the superficial part of the gland.

The muscles having origin or insertion on the framework outlined above complete the musculoskeletal bed of the parotid gland. The mastoid process is hidden from view by the insertion of the sternocleidomastoid muscle on its lateral surface. This muscle completes the posterior margin of the described compartment and is overlapped near its insertion by the superficial portion of the parotid gland.

Helping to fill the incompletely formed medial wall of the fossa is the posterior belly of the digastric muscle and those muscles originating on the styloid process. The digastric muscle originates in a notch medial to the tip of the mastoid process and thus deep to the insertion of the sternocleidomastoid. (Figs. 1 and 2.) In its course obliquely downward and forward, its anterior border overlaps the tip of the transverse process of the atlas; near the hyoid bone its intermediate tendon is surrounded by two limbs of the stylohyoid muscle. (Fig. 2.)

The styloglossus, stylohyoid and stylopharyngeus muscles pass anterior to the transverse process of the atlas and fan out to their insertions from above downward as named. They are grouped together near their roughly common origins, but only the stylohyoid muscle is easily seen in the usual surgical exposure. It is more superficial than the other styloid muscles, possesses a more tendinous origin than the others, and usually is separated from them by the external carotid artery.

Anteriorly, three muscles insert on the bony margin formed by the mandibular ramus. From its origin on the zygomatic arch, the masseter muscle passes to the lower lateral surface of

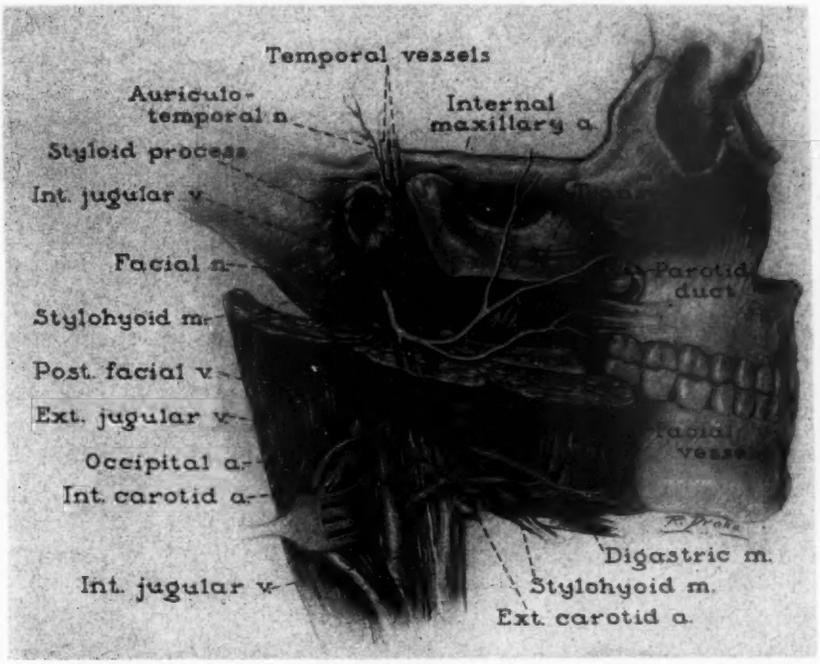

FIG. 2. The regional anatomy of the parotid gland. The interrelations of structures traversing and lying deep to the gland are emphasized.

the ramus and the periphery of the angle of the mandible. Thus completely clothing the external surface of the lower portion of the ramus, the masseter muscle is overlapped to a variable extent by the superficial portion of the parotid gland.

The main bulk of the two pterygoid muscles lies in the infratemporal fossa well anterior to the field of dissection. (Fig. 2.) However, at their insertions they are related to that portion of the parotid gland which wraps around deep to the posterior border of the ramus of the mandible. Specifically, the pterygoideus lateralis runs horizontally backward to insert on the anterior surface of the temporomandibular joint and adjacent neck of the mandibular ramus. The pterygoideus medialis passes obliquely downward and backward to insert on the inner surface of the angle of the mandible. It clothes this side to a lesser extent than the masseter muscle does the lateral surface.

General Form of Parotid. The parotid gland, particularly its superficial portion, varies considerably in size and shape. Molded into and overlapping the recess just described, its general form is irregular. For descriptive purposes, however, it is considered to have four surfaces, namely, superficial, deep, anterior and posterior. The deep surface tapers superiorly and inferiorly, so that borders rather than surfaces are formed.

The posterior surface is grooved by its contact with the anterior border of the sternocleidomastoid muscle, the mastoid process and the external auditory meatus.*

The deep surface of the gland, molded to the medial wall of the musculoskeletal recess just described, bears the impression of the styloid process and its muscles. (Fig. 2.) The tissue posterior to this impression lies against the digastric muscle (and deeper still, as will be described later, a portion of the internal jugular vein). The tongue of tissue anterior to the styloid process may extend deep to the temporomandibular joint. In this location the gland lies deep to the insertion of the pterygoideus lateralis and is separated from the pharyngeal wall by loose connective tissue.

The anterior surface of the gland is grooved by the posterior margin of the ramus of the mandible. The inner lip of this groove reaches for a short distance between the two pterygoid

* The extreme irregularity of the posterior and deep surfaces and the absence of a distinct angle or corner between them (Fig. 2) understandably have led some authors to describe them together as a single "posterior" surface. The gland then becomes a "three-sided wedge," possessing superficial, anterior and posterior surfaces.

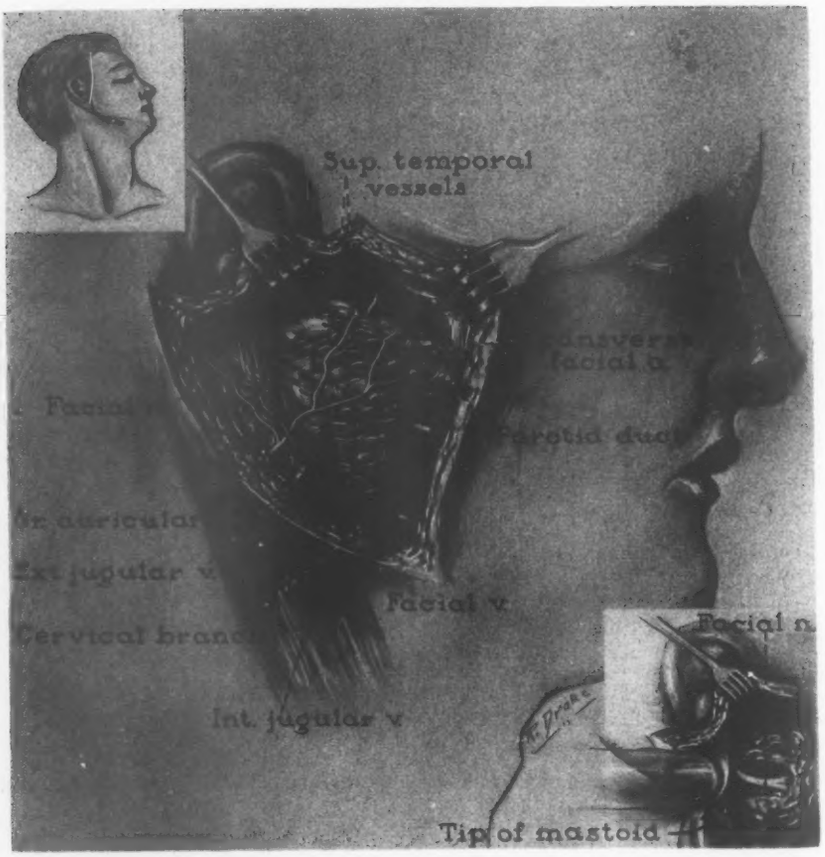

FIG. 3. The operative field as it appears after the cutaneous flaps have been elevated. The anterior flap has been mobilized more than is recommended at this stage of the dissection.

muscles and the outer lip extends for some distance over the surface of the masseter muscle.

The superficial surface of the gland is the largest and most variable in outline. It is generally described, in its most common form, as a triangle with its apex directed inferiorly. (Fig. 3.) Its posterior border overlaps the sternocleidomastoid muscle below, and it may be traced upward first below and then anterior to the external auditory meatus. At a variable level it joins the superior border of the gland, which runs forward below and roughly parallel to the zygomatic arch. The anteroinferior border completes the triangle and overlaps the masseter muscle to a variable extent. For a detailed account of the variations in size of the gland and the shape of its superficial surface, the reader is referred to the excellent anatomic study of McCormack and associates [9]. The same general spatial relationships obtain whether the outline of the superficial surface presents as an oval, an inverted L or a variously oriented triangle.

Related Fascia. The concept of the parotid fascia described by Davis and co-workers [5] best fits the situation found at operation. They considered the gland to be related to a superficial layer and a deep layer of connective tissue that fuse peripherally to enclose it. The outer layer is that fascia which, in the cervical region and the lower part of the face, contains the platysma muscle. The inner layer is actually the investing fascia of the masseter muscle. They further described the continuity of this fascia, with numerous septa passing in among the lobules of the gland, as well as the connective tissue surrounding the intraglandular portion of the facial nerve.

All surgical procedures in the parotid region are facilitated by the existence of these fascial elements. The connective tissue on the superficial surface of the gland provides a cleavage plane useful for its exposure, and the presence

of fascial prolongations within and between the parotid lobules makes possible technics of blunt dissection by which damage to the facial nerve is best averted.

Nerves Adjacent to and Traversing Parotid. Great auricular nerve: Usually the largest branch (C_3) of the cervical plexus, the great auricular nerve bends around the mid-portion of the posterior border of the sternocleidomastoid muscle and ascends on its lateral surface. (Fig. 3.) It generally lies behind and tends to parallel the external jugular vein, but is at times in contact with the vein. At a variable level it divides into mastoid, auricular and facial branches. In the surgical exposure for parotidectomy this nerve or its more anterior branches may be identified 1 to 2 fingerbreadths below the tip of the mastoid process. It is routinely removed during parotidectomy.

Facial nerve: The stylomastoid foramen lies just posterior to the base of the styloid process, between it and the anterior limit of the mastoid notch, which is the groove for the origin of the digastric muscle. (Fig. 1.) After leaving the skull through this aperture, the trunk of the facial nerve passes downward, giving off the small postauricular and digastric branches, and then curves anterolaterally. (Fig. 2.) Early in its extracranial course, as it appears first in front of the digastric muscle and then lateral to the styloid process, it is embedded in parotid tissue. Farther forward, near the point of its major division, it passes superficial to the posterior facial vein and the external carotid artery. In this region, the nerve or its major divisions are usually in contact with the lateral surface of the vein but are separated from the artery by the parenchyma of the gland. (Fig. 2.)

After forming its major temporofacial and cervicofacial branches, the nerve is distributed above to the temporal (ophthalmic), zygomatic and buccal areas and below to the region of the margin of the mandible and the neck. The primary division is constant but considerable variation occurs in the origin, interrelations and specific distribution of the peripheral branches.

The detailed patterns of this variation have been described and classified by several authors. We do not wish to belittle the value of these studies since they have increased the basic knowledge of the entire region. However, in a practical light, the point about the seventh nerve that we wish to emphasize is not the variability of its branching but the constancy of the position of its trunk.

In looking for a useful structure of reference for the trunk, we can analyze the spatial relations already mentioned as the course of the facial nerve was described. Knowledge of these relations is obviously important to the surgeon but none of the structures mentioned is a suitable landmark for identification of the trunk as an initial step in parotidectomy. The styloid process lies deep to the structure we wish to identify and avoid. Moreover, as the anatomic studies of Davis and associates [5] have shown, it is absent in 30 per cent of specimens and is so small as to be shielded by its sheath in another 20 per cent. Even in the remaining 50 per cent of instances it can be palpated or visualized only after considerable dissection in a critical zone.

The vessels already referred to are somewhat variable in position, bear no definite relation to the main trunk of the nerve and, like the styloid process, are exposed within the gland only after much dissection. In fact, the intraglandular portion of the external carotid artery is not visible even after completion of superficial parotidectomy.

The branches of the facial nerve emerging from the periphery of the gland have been used as guides to the main trunk by some surgeons. This practice is feasible but it appears less logical to us than does early identification of the nerve trunk posterior to the gland. The isolation of several small rami that vary in position entails several separate dissections performed without the aid of reliable landmarks. It is clear that greater safety is present in a single dissection in which a sizable structure is sought, particularly when its position is invariable and it is related to an easily demonstrable landmark.

The mastoid process is such a landmark, and we wish to emphasize the constant spatial relation between it and the nerve trunk. The trunk may be identified as an initial step in parotidectomy with the aid of the maneuver illustrated in Figure 3 (lower insert). A finger tip placed as shown on the lateral surface of the process will point directly to the critical zone of dissection. In a plane of dissection maintained immediately on the anterior surface of the mastoid process, no vital structure lies between the finger tip and the stem of the

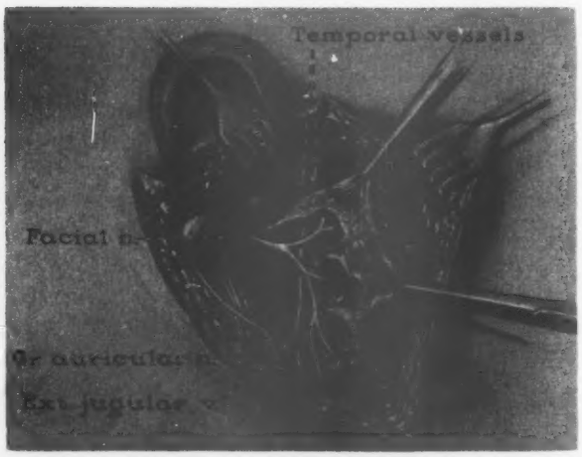

FIG. 4. The trunk of the facial nerve has been identified and the superficial portion of the parotid gland is being dissected free of the nerve rami.

seventh nerve. This dissection will be described more exactly in the section on surgical technic.

Considerable controversy has existed about the exact nature of the structural relations between the facial nerve and the surrounding parotid parenchyma. This anatomic relationship has significance in two separate aspects of surgical intervention in this region, namely surgical technic and the pathogenesis and spread of tumors. Reflection on the differences of opinion found in the literature suggests that they are more apparent than real. Actually, much of the controversy has resulted from confusion between the two separate but related aspects just mentioned, and from the misapplication of arguments.

From the standpoint of surgical technics, it is clear that a definite gross plane of dissection may be developed in the plane of the facial nerve between two portions of the parotid gland. (Fig. 4.) No evidence derived from histologic or embryologic data or from studies utilizing injection of the duct can be used to refute the feasibility of commonly practiced technics based on this practical observation. Such studies are relevant, however, to considerations of surgical treatment as they relate to the origin and spread of tumors. Simply stated, the nature of the structural relationship between facial nerve and parotid parenchyma has significance in two separate therapeutic problems, namely what can be done, and what should be done. The first question is settled but the second remains controversial.*

*A complete comment on this controversy is not within the scope of this paper. We agree with Winsten and Ward [14], who considered the parotid gland to be a unilobar, multilobular structure. Those who disagree with this concept must admit that, regardless of the presence or lack of actual continuity of ducts and parenchyma between the superficial and deep portions of the gland, these two portions are contiguous. To this extent, in the treatment of tumors with invasive characteristics, the gland must be considered as a single structure. However, at present we consider that the surgeon is justified in taking advantage of the gross plane of cleavage that can be developed between superficial and deep portions of the gland when dealing with non-invasive lesions.

Auriculotemporal nerve: Small but significant in its relation to Frey's syndrome, this nerve has its origin in the infratemporal fossa well anterior to the field of dissection. Branching from the posterior surface of the mandibular nerve, it passes backward and slightly downward on the medial surface of the external pterygoid muscle. After bending outward behind the neck of the mandibular ramus just below the temporomandibular articulation, it ascends through or deep to the substance of the parotid gland to take a vertical course just anterior to the external auditory meatus. (Fig. 2.) In this region, anterior to the tragus, the order of structures from behind forward is usually auriculotemporal nerve, superficial temporal vessels and temporal branch of the facial nerve.

Regional Blood Vessels. The variability of the veins in this region and the fact that all may be sacrificed with impunity, including the internal jugular vein if necessary, make a tiring description of detail and variation unjustified. As a basic pattern (Figs. 2 and 3), the superficial temporal and internal maxillary veins unite to form the posterior facial vein. This vein divides (often within the gland) into two branches, an anterior which joins the anterior facial vein to form the common facial vein, and a posterior which unites with the smaller posterior auricular vein to form the external jugular vein. Thus the posterior facial vein drains into two separate systems; it passes directly into the external jugular vein and it drains by way of the common facial vein into the internal jugular vein. The two jugular systems are separated at the level of entry of the common facial vein by the sternocleidomastoid muscle.

Although not vital structures, the veins in the parotid region cannot be ignored in the safe performance of a planned procedure. Knowl-

edge of the following common spatial relations is helpful to the surgeon.

The position of the extraglandular portion of the posterior facial vein may be noted in the superficial dissection shown in Figure 3. The cervical branch of the facial nerve usually lies near it anteriorly but often overlies the vein. This relation should be borne in mind as the skin flaps are elevated and as the deeper dissection is begun if damage to the nerve is to be avoided. Above this level, the vein is surrounded by parotid tissue and lies in the same plane as the facial nerve. (Fig. 4.) Although it is usually in contact with the deep surface of the nerve, this vein may be split by the nerve or its branches.

The anterior facial vein is generally not in contact with the parotid gland and usually lies just anterior to the operative field. (Fig. 3.) If this region is exposed, the surgeon should know that the marginal mandibular branch of the seventh nerve commonly overlies the vein at or below the lower border of the mandible. (Fig. 2.)

Although the internal jugular vein passes deep to the usual operative field in the parotid bed, exact knowledge of its location is important. It leaves the skull just medial to the base of the styloid process (Fig. 1), descends on the lateral wall of the pharynx and lies immediately on the anterior surface of the transverse process of the atlas. Thus it lies deep to two bony landmarks (the styloid process and the tip of the transverse process of the atlas) and deep to the digastric and styloid muscles. (Fig. 2.)

The arteries in the parotid region are subject to less variation than are the veins. The internal carotid artery ascends vertically on the anterior surface of the internal jugular vein. Lying in a plane slightly medial to the vein, it also runs deep to the musculoskeletal bed of the parotid gland.

The external carotid artery is shielded by the angle of the mandible soon after it emerges from beneath the anterior border of the sternocleidomastoid muscle. (Fig. 2.) Unlike the posterior facial vein, which runs superficial to the digastric and stylohyoid muscles, the artery ascends deep to these two muscles and passes between them and the deeper styloid muscles. At first separated from the deep surface of the parotid gland by the digastric and stylohyoid muscles, the external carotid artery then curves gently outward over the upper margin of the latter muscle and enters that portion of the gland which is molded inward in front of the styloid process. (Fig. 2.) The external carotid artery may form its terminal branches in or just above this intraglandular segment, so that on emerging from parotid tissue either it or its terminal branches groove the deep surface of the parotid gland.

The branches of the external carotid artery generally are classified as anterior, posterior, ascending and terminal. However, for the purpose of this description, they are best considered with reference to their levels of origin as related to the digastric muscle and the intraglandular segment of the parent vessel.

The superior thyroid, lingual and ascending pharyngeal arteries make up the first group. They arise well below the posterior belly of the digastric muscle and lie away from the field of dissection for parotidectomy.

The occipital and external maxillary (facial) arteries may be considered together. They usually originate near the lower border of the digastric muscle. (Fig. 2.) Although they pass close to the gland, they are rarely in contact with it and are seldom seen during parotidectomy. The occipital artery runs slightly upward and backward under cover of the digastric muscle; just medial to the origin of this muscle, it grooves the mastoid process and runs posteriorly away from the parotid region. The external maxillary artery ascends obliquely forward deep to the digastric and stylohyoid muscles and arches over the latter muscle. It then grooves the posterior and superior surface of the submaxillary gland as it passes between that structure and the mandible. Becoming superficial, it appears from beneath the ramus of the mandible at the anterior border of the masseter muscle. Here it runs in company with the anterior facial vein, whose more direct and superficial course has been described.

The remaining branches of the external carotid artery are related more intimately to the parotid parenchyma. The posterior auricular artery arises near the upper border of the digastric muscle. (Fig. 5.) It passes backward and upward along or superficial to this border to reach the interval between the mastoid process and the external auditory meatus. Its position on the anterior surface of the mastoid process is surgically significant since it is usually encountered in the dissection to expose the trunk of the seventh nerve.

FIG. 5. The bed of the parotid gland as it appears after total parotidectomy with preservation of the facial nerve.

The internal maxillary and superficial temporal arteries comprise the fourth group of branches. In contrast to the artery just described, which has its origin near the lower portion of the intraglandular segment of the external carotid artery, these vessels are formed near the upper limit of this segment. The internal maxillary artery runs forward deep to the ascending ramus of the mandible (Fig. 5) to lie either deep or superficial to the external pterygoid muscle. The superficial temporal artery grooves the deep surface of the parotid gland as it ascends in front of the tragus, between it and the temporomandibular joint. Its significant branch in this region, the transverse facial artery, passes superficial to the mandibular ramus to reach the cheek. It lies just below the zygomatic arch on the surface of the masseter muscle.

Parotid Duct. Stensen's duct is formed at the anterior border of the gland by the confluence of several tributaries. Accessory glandular tissue may lie on or near it in its early course. It crosses the masseter muscle and turns in sharply at the anterior border of this muscle to pierce the buccinator muscle..

Variations in the distribution of tributary ducts have limited surgical significance. Although salivary fistulas may follow incision of the parotid gland or removal of its lower pole in radical dissection of the neck, they have not occurred in our experience after superficial parotidectomy.

The preceding description of regional anatomy is obviously less comprehensive than are some of the original basic studies recorded in the literature. We have not intended such a study but rather have chosen to emphasize basic anatomic patterns that will be useful to the surgeon. Minor variations will be encountered. The trained surgeon can deal with these just as he does in any other anatomic region. To this extent, we consider that some degree of oversimplification is justified.

SURGICAL TECHNIC

The fundamentals of the procedures to be described are known to many. The details of technic are a synthesis of the contributions of several surgeons and the concepts that have resulted from the senior author's experience in surgical treatment of the parotid gland. It is not possible to assign credit fairly in any field in which the evolution of methods has come from the efforts of many workers. It is likely that the first superficial parotidectomy was performed with an awareness of the basic principles that since have been repeatedly contested, discarded and rediscovered.

According to Kidd [*8*], Carnadine in 1907 is said to have first carried out parotidectomy with preservation of the facial nerve. Barbat [*3*] reported a single case in 1916. Later Sistrunk [*12*] and Adson and Ott [*1*] described a satisfactory technic for parotidectomy. Since that time the contributions of Bailey [2], Janes [*7*], Furstenberg [*6*], State [*13*] and others have been noteworthy. Similarly, the anatomic studies of McWhorter [*11*], McCormack and associates [*9*], McKenzie [*10*] and Davis and co-workers [*5*] have stimulated surgical practice. Numerous surgeons and anatomists not mentioned here are deserving of credit; the reader is referred to the excellent historical review in the article by Davis and associates [*5*].

Preparation of Patient. Although blood transfusions are seldom necessary in operations on the parotid gland, the patient's blood group should be known and facilities for transfusion should be available.

The patient is placed in the supine position with a small pillow beneath his shoulders. During the operation his head is turned away from the side of dissection and the head of the table is elevated to a 45 degree position.

We routinely use general anesthesia with endotracheal intubation for operations in the parotid region.

The draping of the patient, once learned, is more easily done than described. (Fig. 6.) The

regional skin is prepared in the usual manner and two sterile towels are placed beneath the head. The lower of these extends a short way beneath the patient's shoulders and is left undisturbed. The lower border of the upper towel is placed beneath the occipital protuberance. This towel is wrapped about the head and clipped to itself over the endotracheal apparatus at the level of the eyebrows, leaving the ear on the operative side fully exposed. A sterile towel is then placed longitudinally on each side of the neck. The medial border of each overlaps the towel on the head just behind the ear and extends down over the thorax. (In Figure 6 these longitudinal towels are covered by folded towels tucked in between them and the patient's neck.) The top edge of a large sheet covers the patient and instrument table and reaches up to the lower part of the neck.

A folded sheet covering the head is arranged as follows. The mid-point of the crease at its lower border is clipped to the chin. On the side to be dissected, this edge of the sheet is fixed to the towel encircling the head just above the eye with a curved hemostat. In this way the cheek and the corners of the eye and mouth are included in the operative field. This same edge of the sheet is next fastened to the towel on the head just behind the ear and care is taken that the longitudinal towel on this side is included in the grasp of the curved hemostat. Thus three drapes are fixed securely at their point of junction behind the ear. Lateral to this point a towel clip fastens the sheet to the bottom head towel and the underlying pillow. Sufficient slack is left between this clip and the last curved forceps to allow for rotation of the head to the opposite side.

Only one forceps is used on the opposite side to join the towel on the head, the longitudinal towel and the sheet, since the ear need not be exposed. The sheet is clipped to the underlying pillow as on the other side, and the draping is completed as the sheet covering the patient's body is fastened to the two longitudinal towels where their borders intersect on the lower part of the neck.

The Incision. The Y, or inverted T, incision shown in Figure 3 (upper insert) and Figure 6 allows excellent exposure of the parotid region when the anterior and superior cutaneous flaps are fully mobilized. Its major limb is begun behind the external ear and about 2.5 cm. above

FIG. 6. The recommended drape for operation on the parotid gland. The proposed incision has been outlined.

the tip of the mastoid process. It is then extended downward and forward in a gentle curve, passing just behind and below the angle of the mandible. It is carried forward to end about 2.5 cm. anterior to this angle. The anterior (minor) limb of the Y incision is made to lie in a natural crease of the skin in front of the ear. It extends from the level of the tragus to its junction with the primary incision about 1 cm. below the base of the ear lobe. The minor and major limbs of the incision should join at a right angle.

Elevation of Skin Flaps. Tension is applied across the epidermal incision and it is deepened until "give" is felt as the corium is divided. The anterior flap is elevated first. Rake retractors are placed in the skin and strong outward traction is maintained as the proper plane of dissection in the investing fascia of the gland is sought. This cleavage plane is best developed and carried forward by scissors dissection, with alternate spreading and cutting. As the superficial surface of the gland is exposed, the surgeon applies firm digital pressure to it through a folded gauze sponge. This controls bleeding and provides countertraction to the rake retractors in the skin.

During this part of the dissection one encounters numerous filaments of connective tissue that pass from the surface of the gland to the anterior skin flap. Their resemblance to nerve filaments may disturb the surgeon unless it is realized that nerve rami are present only at the periphery of the gland.

Two additional points may be made in this regard. First the anterior flap is mobilized only up to the periphery of the gland at this time. There is less risk of damaging the distal branches of the facial nerve if this part of the dissection is carried out after the main trunk of the nerve has been identified posterior to the gland. Secondly, since the lower portion of the cutaneous incision usually lies at or below the lower pole of the gland, this part of the flap must be mobilized cautiously if the cervical branch of the seventh nerve is to be identified and preserved. Its position, which is superficial or just anterior to the posterior facial vein, must be kept in mind.

The superior cutaneous flap bearing the ear lobe is elevated next. Here, as before, firm upward and outward traction with rakes greatly facilitates the identification and maintenance of the proper cleavage plane. After this dissection has been carried up to the external auditory meatus, the posterior border of the superficial surface of the parotid gland may be identified and freed superficially. The deeper dissection in this region (between the gland and the posterior wall of the musculoskeletal recess) is best deferred until the remaining skin flap has been raised.

Since the skin posterior and inferior to the primary incision has a concave margin, it is not truly a flap. It cannot and need not be mobilized as fully as are the two flaps. However, it should be elevated sufficiently to permit identification of the great auricular nerve and the external jugular vein. These structures are divided and the position of the cervical branch of the facial nerve is kept in mind as the dissection is carried deeper around the lower border of the parotid gland to identify the mid-portion of the posterior belly of the digastric muscle.

Before the next step of the procedure is undertaken, it may be necessary to ligate any bleeding vessels that might interfere with clear visualization of the trunk of the facial nerve as the posterior surface of the gland is mobilized. During the dissection just described an occasional spurting artery will require ligation, but the major part of the bleeding is of venous origin and may be controlled with traction and pressure. When this point in the dissection is reached, it is surprising to see that a nearly dry field has resulted from these measures and the passage of time. After the few sites of persistent bleeding have been controlled, the surgeon may proceed with the dissection for identification of the trunk of the seventh nerve.

Identification of Trunk of Facial Nerve. The lowermost tip of the mastoid process now can be palpated easily through the insertion of the sternocleidomastoid muscle. A finger tip is placed on the lateral surface of the process pointing directly forward. (Fig. 3, lower insert.) Care is taken that the inferior surface of the digit lies flush with the tip of the mastoid. With the rare exception to be mentioned presently, the trunk of the facial nerve will be found to be deep and slightly anterior to the center of the finger tip so placed. Thus the operator's critical attention may be focused in a limited zone of about 1 cm.

The previously identified posterior border of the gland is now grasped with two or three Kocher's forceps and is retracted forward and outward as a plane of dissection is developed between the posterior surface of the gland and the structures it abuts (Fig. 4), namely, the sternocleidomastoid muscle, the mastoid process, the cartilaginous portion of the external auditory meatus and, deeper, the posterior belly of the digastric muscle. Seldom can the posterior auricular artery be isolated prior to its division. It is the sole source of brisk bleeding in this region and it usually can be controlled temporarily with pressure and traction. Ligature by suture is avoided until one is certain he is away from the stem of the seventh nerve. The plane of dissection is best developed with small blunt-tipped scissors, such as the Jones dissection scissors, alternately pushing parotid tissue away from the structures behind and cutting cautiously.

As the dissection is carried deeper, the anterior surface of the mastoid process is felt to curve posteriorly. At this point, if the palpable tumor lies away from this immediate region, the trunk of the nerve is found most easily by directing the plane of dissection somewhat anteriorly through glandular parenchyma. Since the nerve curves laterally as well as forward as it descends from the stylomas-

toid foramen, it is less deeply placed when exposed at this point about 1 cm. in front of the mastoid process. Thus its exposure is simplified by use of this technic. Damage to the nerve is averted if the force of blunt dissection is directed from behind forward in the axis of the nerve and if the retracted gland is kept under firm tension. The stem of the nerve often can be palpated before it is seen.

Before the next step of the procedure is described, an alternate method for location of the nerve should be mentioned. If the technic just recounted is used, a small wedge-shaped portion of the superficial part of the gland is left in place. This is not advisable if the lesion involves this part of the gland or if the tumor is suspected of being invasive. In dealing with tumors of this sort, the dissection should be maintained on the posterior surface of the gland. In this way the nerve is located at a slightly deeper level and parotid tissue is not transected.

This latter technic also should be used in treating tumors of the deep portion of the gland, since lesions in this location may alter the more distal course of the nerve trunk. In such cases the proximal portion of the trunk bears the more constant relation to the suggested landmark.

Removal of Superficial Portion of Parotid. After the trunk of the seventh nerve has been isolated, the dissection is carried forward in the plane of its branches. Again, outward and forward traction is exerted on the superficial lobe by means of Kocher's forceps. (Fig. 4.) Bit by bit this block of tissue is lifted free of the nerves and interposed deep parenchyma by use of the closed tip of small blunt dissecting scissors. Although contraction of the facial musculature may be seen during this maneuver, stimulation of this order does not cause significant or permanent damage to the seventh nerve. In fact, observations of muscular twitching may aid in the identification of questionable filamentous structures. However, intentional stimulation of the nerve is seldom necessary. The nerve is a definite structure and in usual circumstances should be identified solely by its appearance.

The nerve will not be injured if it is kept under direct vision, if the plane of dissection is maintained superficial to it, if the force of blunt dissection is directed in the axis of its branches and if the superficial lobe is retracted firmly away from the deeper structures. The importance of pressure and traction cannot be overemphasized; the resulting tension on tissues minimizes the problem of hemostasis and simplifies the difficulties in identification and maintenance of cleavage planes.

As the anterior border of the superficial lobe is freed, the parotid duct is identified, divided and ligated, and any accessory glandular tissue is removed with it. Pressure is removed from the surface of the deep portions of the gland and persistent bleeding points are controlled under direct vision with mosquito hemostats and fine ligatures. If the nerve and its branches are inspected at this time, the surgeon will be impressed by the relatively small size of the peripheral rami. The difficulty that might be anticipated in isolating these tiny branches early in the procedure becomes obvious.

Removal of Deep Portion of Parotid. We consider that treatment by superficial parotidectomy is adequate for non-invasive lesions confined to the superficial portion of the gland. However, if such a tumor originates in or extends into the deep lobe, or if an invasive lesion is present, total parotidectomy is indicated.

If biopsy of a questionable lesion shows it to be non-invasive and if it is confined to the deep lobe, this portion of the gland may be dealt with after the superficial dissection is completed. Since the intraglandular segments of the posterior facial vein and external carotid artery must be removed with the remaining tissue, these vessels are divided and ligated at the lower border of the deep portion of the gland. Similarly, their tributaries must be secured at the periphery of the remnant of the parotid. The superficial temporal vessels are divided superior to the gland and the internal maxillary and transverse facial arteries are severed at its anterior border. With nerve hooks, the branches of the nerve are retracted gently and the deep portion of the gland is removed through a suitable interval between them. This approach will vary with the specific pattern of branching encountered, but usually the tissue is best removed from the space between the major divisions or from below the lower division. It is obvious that an intimate knowledge of the anatomy of the parotid bed is helpful in the performance of deep lobectomy. The appearance of the operative field at the completion of the procedure is shown in Figure 5.

Non-invasive lesions involving both parts of the gland should be managed somewhat differently, if possible, since superficial parotidectomy in such cases may result in the transection of tumor tissue. The usual plane of dissection is established through normal parenchyma, but the continuity of neoplastic tissue between superficial and deep portions of the gland is left undisturbed in the affected zone. Although this ideal technic is often feasible, it is made impossible at times by difficult exposure. The main bulk of the tumor occasionally will come away with the superficial portion of the gland, leaving gross or microscopic extensions of tumor tissue in the remaining deep parenchyma. In this event, removal of the superficial portion of the gland will not have resulted in clean removal of the tumor with a sufficient margin of unaffected tissue, and the procedure must be completed as a total parotidectomy with preservation of the facial nerve. Such piecemeal removal is an imperfect surgical technic; however, the risk of cellular implantation must be accepted in dealing with histologically benign lesions when the only other alternative is sacrifice of the facial nerve. This risk may be minimized by careful excision of all evident parotid tissue and irrigation of the operative site at the completion of parotidectomy.

The proper treatment of invasive tumors of the parotid gland entails willful sacrifice of the facial nerve. The anatomy and the surgical technic described are easily applied in this situation as total parotidectomy is performed. The technic for re-establishment of function of the seventh nerve using nerve grafts has been presented by one of us (O. H. B.) and L'Esperance [4] in an earlier publication.

COMMENTS

The procedures described in this paper have been presented purposely in a specific and didactic manner. It is obvious that certain situations must be met with individualized modifications of these basic technics. In this regard, experience with the recommended approach has shown it to have a desirable degree of flexibility. The basic methods may be applied to any situation encountered in surgical treatment of the parotid gland, whether its solution entails biopsy, superficial parotidectomy, or total parotidectomy, with or without preservation of the facial nerve.

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The Relation of Concomitant Disease to the Occurrence and Management of Trauma

CHARLES S. TANNENBAUM, M.D., *St. Louis, Missouri*

From the Department of Surgery, Harvard Medical School and the Surgical Service, Massachusetts General Hospital, Boston, Massachusetts. This study has been sponsored by the Commission on Accidental Trauma of the Armed Forces Epidemiological Board, Department of Defense, and supported in part by funds from the Office of the Surgeon General, Department of the Army.

ACCIDENTAL trauma is becoming an ever increasing cause of death and hospitalization in Western civilization. It is the leading cause of death in the twenty to forty year age group in this country. In 1954, there were (exclusive of experience among the armed forces overseas) 10,000,000 accidents and 90,000 deaths in the United States due to this cause, a rate of 55.9 per 100,000 population [2]. Of these deaths, 36,000 occurred as a result of motor vehicle accidents, and 20,000 were secondary to accidental falls. Every surgeon has treated patients in whom there existed some concomitant disease state not produced by the trauma. This often caused the accident and materially influenced the patient's welfare and the choice of therapy. The literature of the past ten years contains few references to the role of such concomitant disease in the production and management of accidental injury.

One study, for example, discussing the epidemiology of accidents includes host, agent and environmental factors in causation, and lists race, sex, age and "genetic inherent susceptibility" as host factors, but makes no mention of disease itself as a possible contributing factor [13]. An excellent review of automobile accidents gives but passing reference to the " . . . occasional contribution of chronic illness to auto accidents" [21]. In these and other such studies, there is no quantitative estimate of the role of concomitant disease in the production or surgical management of trauma.

The experience with cases of trauma among the municipal hospitals of New York City in 1954 has been described, but here too no attempt at full description of diagnoses upon discharge was made [10]. The most comprehensive attempt to examine the role of concomitant disease and its association with accidents was by Collins, Phillips, and Oliver [6], who studied a health district of Baltimore from 1938 to 1943 using house-to-house personal interview. In this study, the relationship of chronic disease to accident liability was investigated. Information pertinent to disease morbidity was obtained by questioning at home and by consulting the family physician when uncertainties arose. The disease considered to be of primary importance, when several were present, was the one "which usually involves the most disability and medical care or the greatest risk of death or permanent disability to the patient." "Major" chronic disease was defined as cardiovascular disease, arthritis and chronic rheumatism, mental disease or defect, and "others." Although chronic disease was more prevalent among those experiencing repeated accidents during the five year interval, there was no statistically significant difference (among those with major chronic disease) between the number of persons who did and those who did not have accidents. The authors point out that: "The logical statistical approach . . . would be to divide the observed population into those who had no chronic disease, and groups with certain chronic disease, and then compute accident rates for persons in each group. In other words, the absence or the presence of specific chronic disease would be the independent variable." From the viewpoint of the surgeon interested in trauma, this study is deficient in that its basic population is not

one consisting of hospitalized injured persons [7].

Industry has become increasingly interested in the health of workers as a measure of accident proneness. A typical study along these lines appeared in 1950 and reviewed the health of 297 workers in a stamping plant who had experienced ten or more accidents in one year [24]. Of these 297 people seven had faulty vision, thirteen had cardiovascular or renal disease, chronic arthritis, and "other diseases which may have increased their accident rates. A few are known to be chronic alcoholics."

Some attention has been paid to certain specific conditions and the part they play in some trauma. "Accessory" findings in a small series of traffic fatalities of people aged fifty or more were reported [18], and it was noted that "some of the accessory findings were of special interest from the standpoint of driver proficiency and licensing." The relationship between alcoholism and automobile accidents has received increased attention recently both in medical literature and in the lay press [9,14]. One county coroner reported that in each of three successive years 40 per cent of all subjects of traffic fatalities at autopsy had postmortem blood alcohol levels high enough to "impair the efficiency of the person and thus contribute to the fatality" [12]. Bennett [4] alleges that people with multiple sclerosis have an increased accident liability. Three cases of automobile accidents arising directly as the result of grand mal attacks in drivers appeared in the French literature in 1955 [3]. The authors [3] make a plea for routine histories, physical examinations, and electroencephalography among professional drivers.

Most attention in examining the role of concomitant conditions in accident production has been paid to sickness in the aged. In this group and in the very young, two facts have become clear; first, the highest accident case fatality rates occur in the very young and the very old in the United States [23] and in England [5]; and second, the accidents in these groups are easier to study because of the more limited environments in which these persons operate as compared to those of other age groups. In persons aged sixty or over, accidents were responsible for 213 deaths per 100,000 population in 1954 or approximately four times the accident death rate for the over-all population of the United States. Kennedy [17], in discussing accidents among the elderly has noted that, "the whole problem of management of the aged individual who has suffered an injury includes many important and even critical factors not usually stressed in younger persons." He points out the importance of determining whether cerebral trauma is the result of something other than the known external force associated with the accident. General and local muscle paresis, Parkinsonism and syncope [16], and minor cerebrovascular accidents [1] have been cited as conditions sometimes causing falls among the elderly. In 1955 a British study [8] reviewed severe falls occurring in people age sixty or older in one health district during one year. Of those who fell, 41 per cent were considered subsequently as having been "unfit" at the time of the accident, and of those persons aged sixty or over who had not fallen during the year, 18 per cent had been unfit, and the authors concluded that "the subjects who fell were as a group less fit than the rest." The lack of adequate definition of "fit" and "unfit" in this study detracts from the usefulness of the findings. Accident prevention among children has been approached from the point of view of the psychiatrist [18]. No other studies including childhood disease as trauma-producing factors are available.

Studies of the foregoing type and the increasing number of accidents have stimulated more attention to the place of the medical profession in accident prevention, in addition to care of the injury itself. A prominent physician–life insurance executive has said: "The physician can make an important contribution to the prevention of accidents by recognizing these factors and doing everything possible to eliminate them or aid the individual to avoid injury inviting situations." [23]

An editorial in *The Journal of the American Medical Association* [10] in 1952 advised that physicians warn drivers of the increased possibility of automobile accidents when certain illnesses are present. In the elderly, the importance of the family physician in performing careful physical examinations has been stressed. In this way unsuspected factors predisposing to accidental injury might be uncovered [25].

Previous reports have shown the increasing importance of accidental trauma as a leading cause of death in this country [2]. The relationship between certain chronic diseases and in-

creased accident liability in the elderly [*1,23,25*] as well as in all age groups [*1,3,9,10,14,16,18*] has been discussed. No reports have appeared concerning the possible association of such pre-existing disease with the production or management of accidental trauma in a hospitalized injured population. The surgeon who assumes responsibility for the management of trauma finds no information regarding the part played by concomitant disease in the total picture of the hospitalized injured person.

In order to examine quantitatively the importance of concomitant disease in both the production and the management of accidental trauma, a series of admissions for traumatic injury to a large general hospital was studied.

MATERIALS AND METHODS

The records of two groups of admissions to the wards of the Massachusetts General Hospital, from October 1, 1955 through September 30, 1956 were reviewed and compared. Admission via the Emergency Ward was a prerequisite for inclusion in the study. One group of patients called "traumatic" had been admitted because of accidental trauma sustained no longer than two weeks prior to admission. The records of every other admission satisfying these criteria within the year were examined. A control group, called "non-traumatic" was also reviewed. Patients in this category represented all other admissions via the Emergency Ward during the same interval. Every such non-traumatic patient admitted on the fifteenth day of each of the twelve months from October 1, 1955 through September 30, 1956 was reviewed. Patients in both categories were excluded from the study if at least one of the following situations occurred: (1) transfer to semi-private or private services; (2) incomplete record; (3) lost or inaccessible record; (4) previous therapy for the injury at another hospital; (5) lack of at least one report of full history and physical examination (including hemoglobin level, complete urinalysis, and stool guaiac determination); or (6) discharge against attending physician's advice.

No subjective interpretation of material contained in the records was made except in one category as noted herein. Information not available in a category was noted as "not recorded" for that particular case. In the traumatic cases, the following information was noted: age; sex; date of admission; place of residence; circumstances of injury; duration of hospitalization; diagnoses of traumatic and concomitant disease on discharge; degree of association of concomitant diagnosed disease with the production of trauma (here history, physical examination, diagnoses and consultant's opinion were subjectively considered) and cause of death if patient died during this hospitalization. In the non-traumatic case, age, sex, place of residence, date of admission, duration of hospitalization, and cause of death (if death occurred during hospitalization), were noted. The traumatic and non-traumatic samples were compared with respect to the following: rate of exclusion, place of residence, composition of series by age, and by sex in given ages, and duration of hospitalization by age group. Data tabulated for the trauma group alone included: (1) etiology of trauma (i.e., type of accident) by age group and for the entire series; (2) age distribution of patients by the injuries produced; and (3) reported diagnosed concomitant disease (*a*, by amount and type in each age group; *b*, by number of cases requiring immediate evaluation of concomitant disease at time of admission; *c*, by age specific frequency of diagnosis; *d*, by describing cases in which there was positive contribution to the production of trauma). All deaths during hospitalization in both the trauma and the non-trauma group were briefly described. Conventional tests of statistical significance [*15,20*], were used where applicable.

RESULTS

Comparisons between Traumatic and Non-traumatic Groups

Size of Samples. There were 437 traumatic and 163 non-traumatic cases originally chosen, and of these sixty-two and thirty cases respectively, were excluded for reasons mentioned above. The final samples consisted of 375 and 133 cases, respectively. The rates of exclusion in the two groups was not statistically significant (P greater than .05).

Places of Residence of Sample Populations. Distribution of patients in both groups by place of residence is presented in Table I. The compositions of the groups with regard to places of residence was not significantly different.

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Composition of the Two Samples by Age and by Sex. Age composition: Table 11 and Figure 1

TABLE I
COMPOSITION OF GROUPS BY PLACES OF RESIDENCE

Type of Case	Boston		Metropolitan Boston		Others		Total No. of Cases
	No.	%	No.	%	No.	%	
Traumatic.....	193	51.7	144	39.6	37	10.3	374*
Non-traumatic..	59	44	56	42	18	16.0	133

* One undetermined.

show the composition of the two groups with regard to age. There was no statistically significant difference between the two groups in this respect.

Age-specific sex composition: Table III shows the sex distribution according to the various ages of patients in both the traumatic and non-traumatic sample. Only in the traumatic sample was there evidence that one or more age groups differed significantly in their sex composition from the sex composition of the group as a whole (56 per cent males, 44 per cent females). The male to female ratio in each sample was identical.

There were 285 males encountered in both samples and 210 or 74 per cent were traumatic. Seventy-five or 26 per cent were non-traumatic. Statistical analysis shows that in one or more age groups the ratio of traumatic males to non-traumatic males differed significantly (i.e., there was less than 5 per cent possibility that the difference occurred by chance), from the 74:26 ratio previously cited. This phenomenon also occurred among the females.

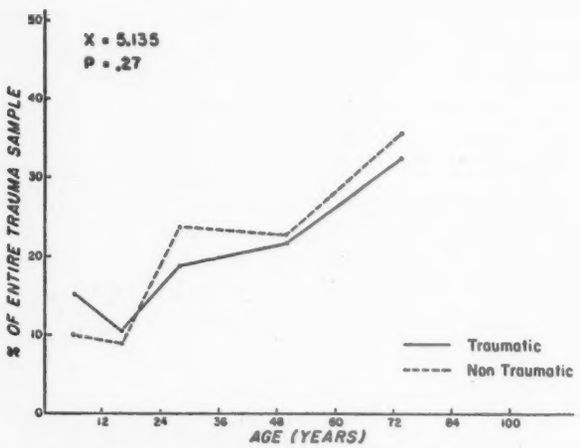

FIG. 1. Age composition of total series of patients.

TABLE II
COMPOSITION OF TRAUMATIC AND NON-TRAUMATIC SAMPLES ACCORDING TO AGE OF PATIENTS

Traumatic Sample			Non-traumatic Sample		
Age (yr.)	No. of Cases	Total Sample (%)	Age (yr.)	No. of Cases	Total Sample (%)
0–9	58	15	0–9	13	10
10–19	42	11	10–19	10	8
20–39	70	19	20–39	32	24
40–59	81	22	40–59	29	22
60 and over	124	33	60 and over	49	37
Totals....	375	100	.....	133	100+

Duration of Hospitalization. The mean duration of hospitalization experienced by the various age groups for the traumatic and non-traumatic samples can be seen in Table IV. Application of the "t" test of significance of differences in a normally distributed population revealed that only among those patients sixty years of age or older was the difference in mean duration of hospitalization between traumatic and non-traumatic persons significant. In this age group the duration of hospitalization of the traumatic group was almost double that of the non-traumatic group.

TABLE III
AGE-SEX COMPOSITION OF TRAUMATIC AND NON-TRAUMATIC GROUPS

Traumatic Sample						Non-traumatic Sample					
Age (yr.)	Males		Females		Total	Age (yr.)	Males		Females		Total
	No.	%	No.	%			No.	%	No.	%	
0–9	40	69	18	31	58	0–9	7	54	6	46	13
10–19	29	69	13	31	42	10–19	4	40	6	60	10
20–39	53	76	17	24	70	20–39	16	50	16	50	32
40–59	46	57	35	43	81	40–59	17	59	12	41	29
60 and over	42	34	82	66	124	60 and over	31	63	18	37	49
Total	210	56	165	44	375	.....	75	56	58	44	133

Data Pertaining to the Traumatic Group Alone

Etiology of the Trauma. Among the 375 persons in the trauma sample, 213 had fallen,

TABLE IV

MEAN DURATION OF HOSPITALIZATION BY AGE OF PATIENT

	Age (yr.)				
	0–9	10–19	20–39	40–59	60 and Over
Traumatic (days)	9.4 ± 2.1	7.4 ± 3.6	9.7 ± 1.8	10.7 ± 6.5	17.1 ± 1.5
Non-traumatic (days)	5.3 ± 4.5	4.5 ± 1.7	5.8 ± 1.3	9.8 ± 2.4	10.7 ± 1.5

thirty-six had been in an automobile involved in an accident, thirty-four were hit by a motor vehicle, and thirty-two had suffered other types of body contact. Sixty were the victims of other incidents. Table v shows causes of

TABLE V

ETIOLOGY OF TRAUMA BY AGE OF PATIENT

Cause of Trauma	No. of Patients by Age (yr.)					Total
	0–9	10–19	20–39	40–59	60 and Over	
Fall	29	16	17	47	104	213
Automobile accident	3	5	20	6	2	36
Hit by car	12	2	5	5	10	34
Body collision	0	9	14	9	0	32
Stab wound	0	2	2	0	0	4
Convulsion	1	0	1	0	0	2
Loss of consciousness	0	0	6	3	6	15
Explosion	0	1	0	1	0	2
Fire	3	2	1	3	0	9
Gunshot wound	0	2	1	1	0	4
Falling weight	1	1	1	2	0	5
Thermal burn	5	0	0	0	0	5
Machinery	1	2	1	1	0	5
Miscellaneous	3	0	1	3	2	9
Total	58	42	70	81	124	375

trauma in the sample, by absolute frequency and by age specific frequency. The most striking fact it demonstrates is that of all the falls which occurred, 49 per cent occurred in the group of people sixty years of age and over.

Frequency and Age Distribution of Patients among the Resultant Diagnosed Injuries. Figure 2 shows the frequency of the various injuries diagnosed among all 375 cases of trauma. Of 418 diagnosed injuries, 55 per cent were fractures, 11 per cent were integumental, 11 per cent were intracranial, 9 per cent were lacerations and 13 per cent were other types.

Figures 3 and 4 show the age and sex distribution of the patients with definite diagnosed injuries, classified by nature and location. The most striking sex differential occurred in the group aged sixty or older. In this group women sustained 73 per cent of all fractures of the extremities, whereas the men sustained 27 per cent. Although this may represent a significant

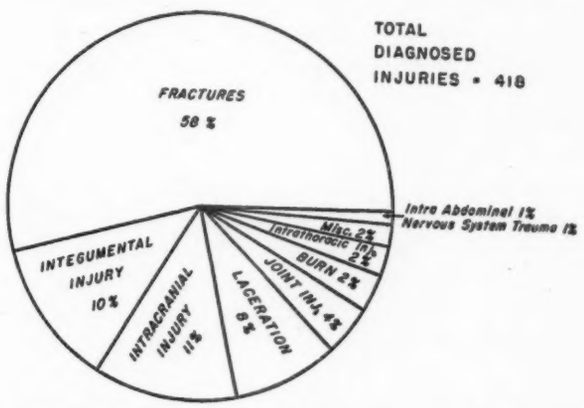

FIG. 2. Relative frequency of various traumatic injuries encountered (when diagnosed) expressed as per cent of all injuries.

difference, the numbers involved were too small for application of tests of significance.

Reported Concomitant Disease among Traumatic Patients. Age specific frequency: Of the 375 traumatic case records, 355 contained a summary of treatment and diagnoses at discharge from the hospital and twenty were incomplete in this respect. The twenty cases were distributed in numbers too small for comparison of non-reporting of diagnoses in one age group as compared to another. Table vi illustrates the age distribution (among cases having summary at discharge) of patients with unequivocally diagnosed concomitant conditions. Some, if not all, of the differences in age specific rates of reporting of concomitant disease could have occurred by chance with odds of less than 1 to 100. In general, the older the person, the more likely he was to

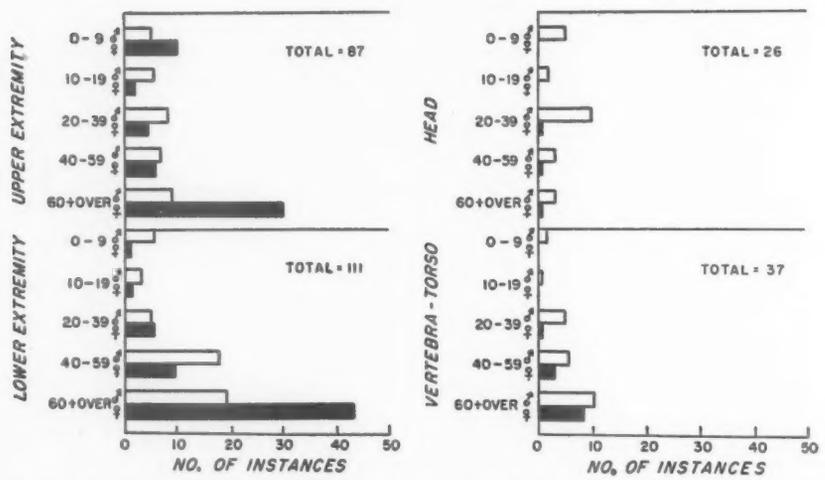

FIG. 3. Age and sex variation of patients, according to fractures experienced.

have had at least one concomitant disease diagnosed and reported.

Table VII lists the categories of concomitant diseases that were diagnosed by frequency of diagnosis in each age group. Once again it is seen that the older the age group the more diagnoses were made, the two striking features being the relatively large number of cardiovascular and gastrointestinal conditions diagnosed and reported in the elderly group.

Evaluation and treatment of concomitant disease at time of admission for traumatic injury: Of 355 traumatic patients with complete summaries at discharge, thirty-three (9.2 per cent), had concomitant diseases which by optimum management standards should have required evaluation and therapy at the time of admission. Table VIII lists these conditions.

Contribution of diagnosed concomitant disease to production of trauma: From the recorded histories, physical examination and opinions of consultants, concomitant disease when it existed in a patient was noted as having 0 (no relation to trauma production), ± (possible relation), or + (definite relation) positive association with the production of traumatic injury. The data are indicated in Table IX. Note the large number of possible cases in the group of patients aged sixty or older, a fact that will be discussed herein.

Among the 355 records of patients who had completed summaries at discharge therefore, at least 8.2 per cent of these people had sustained injury at least partly because of the presence of concomitant disease. Only those traumatic cases in which there was a "plus"

TABLE VI

AGE VARIATION IN REPORTING OF CONCOMITANT DISEASE: PATIENTS WITH DEFINITE DIAGNOSES ONLY

Age (yr.)	Patients with Discharge Summary	Patients with No Concomitant Disease Reported	Patients with Concomitant Disease		No. of Patients According to No. of Concomitant Diseases Diagnosed per Case				
			No.	%	1	2	3	4	5
0–9	53	52	1	2	1	0	0	0	0
10–19	41	41	0	0	0	0	0	0	0
20–39	65	53	12	18	10	2	0	0	0
40–59	77	61	16	21	7	6	1	2	0
60 and over	119	73	46	39	21	14	7	2	2
Total.....	355	280 (79%)	75	21	39	22	8	4	2

TABLE VII
AGE DISTRIBUTION OF PATIENTS WITH REPORTED UNEQUIVOCAL CONCOMITANT CONDITIONS

Category of Condition	No. of Patients According to Age (yr.)					
	0–9	10–19	20–39	40–59	60 and Over	Total
Alcoholism	..	..	2	7	2	11
Anemia	..	..	..	1	2	3
Bone and joint	..	..	1	2	6	9
Cardiovascular	..	..	1	1	36	38
Gastrointestinal	..	..	..	1	11	12
Genitourinary	..	..	..	..	6	6
Malignancy	..	..	..	1	3	4
Metabolic (diabetes mellitus)	1	..	1	..	5	7
Neurologic	..	..	6	6	6	18
Ocular	..	..	..	..	3	3
Psychiatric	..	..	1	1	..	2
Respiratory	..	..	..	3	6	9
Toxic	..	..	..	1	..	1
Miscellaneous	..	..	2	6	2	10
Total	1	0	14	30	88	133

TABLE VIII
CONCOMITANT CONDITIONS REQUIRING EVALUATION AND CARE AT ADMISSION*

Acute and chronic alcoholism	13	Chronic renal disease and uremia	1
Convulsive disorders	8	Delirium tremens	1
Diabetes mellitus	5	Depression	1
Gonorrheal arthritis	1	Electrolyte depletion	1
Barbiturate intoxication	1	Metastatic carcinoma of breast	1
Bronchopneumonia	1	Pneumonia	1
Subarachnoid hemorrhage	1		

* Thirty-two patients with one concomitant condition, one patient with three such conditions.

contribution to injury from concomitant disease had been considered. In no age group was there significant difference between the numbers of those patients having one and those having had more than one concomitant disease

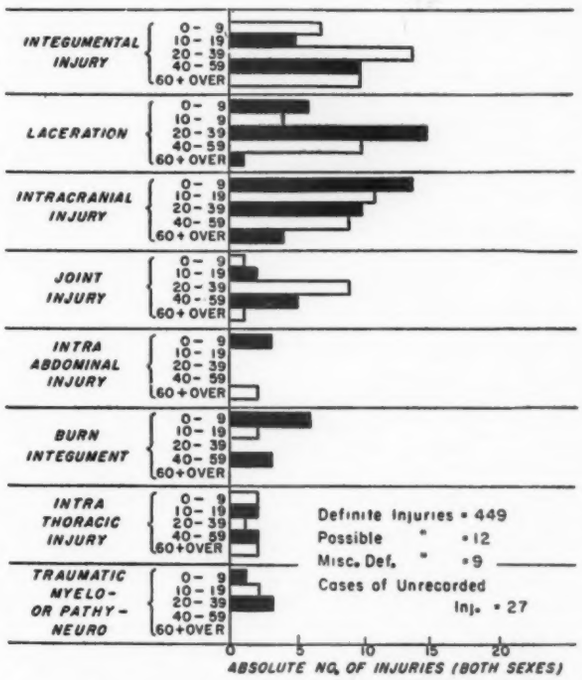

FIG. 4. Age variation of patients according to frequency of all definite traumatic injuries by type and/or location, excluding fractures.

diagnosed and reported. In other words, it seemed that the nature of, rather than the number of concomitant diseases, was the predisposing factor to production of trauma. Table x describes all patients having positive contribution to trauma by concomitant disease.

TABLE IX
DEGREE OF CONTRIBUTION TO TRAUMA BY CONCOMITANT DISEASE (AGE SPECIFIC FREQUENCY)

Age (yr.)	No. of Patients with Discharge Summary	No. of Patients with Diagnosed Unequivocal Concomitant Disease	No Contribution	Possible Contribution	Definite Contribution	Definite Contribution (%)
0–9	53	1	1	0	0	0
10–19	41	0	0	0	0	0
20–39	65	13	3	0	9	14
40–59	77	18	2	2	12	15.5
60 and over	119	46	26	12	8	6.17
Total	355	78	32	14	29	8.2 ($^{29}/_{355}$)

TABLE X

PATIENTS HAVING POSITIVE CONTRIBUTION TO TRAUMATIC INJURY BY REPORTED CONCOMITANT CONDITION

Age (yr.)	Concomitant Condition	Event	Result
23	Epilepsy, grand mal	Syncope	No discharge summary
29	Epilepsy, grand mal	Collapse	No discharge summary
29	Epilepsy, grand mal	Collapse	No discharge summary
29	Epilepsy, idiopathic	Fall	No discharge summary
30	Epilepsy, idiopathic	Fall	Subdural hematoma
32	Epilepsy, idiopathic	Collapse	Fractured femur
34	Chronic alcoholism with toxic psychosis	Fall	Fractured humerus
34	Chronic alcoholism	Fall	Acromioclavicular separation
39	Diabetes mellitus	Body collision	Ischemic ulcer
44	Barbiturate intoxication	Falling weight	Corneal laceration
44	Alcoholism and residual hemiparesis	Collapse	Fractured skull
44	Gonorrheal arthritis	Fall	Septic arthritis
44	Alcoholism and pneumonia with electrolyte depletion	Fall	No discharge summary
45	Reactive depression	Attempted suicide	Bullet wound in temple
48	Chronic alcoholism	Fall	Bimalleolar fractured ankle
48	Chronic alcoholism	Fall	Fractured skull
50	Arteriosclerotic brain disease with occlusion of post-cerebral artery	Fall	Head injury
53	Epilepsy	Collapse	Laceration of the scalp
55	Chronic alcoholism	Hit by car while intoxicated	Fractured femur, metatarsal
58	Metastatic carcinoma of the breast	Fall	Pathologic fracture of the femur
59	Acute and chronic alcoholism	Fall	Laceration of the head
61	Chronic alcoholism	Fall	Fractured clavicle, ribs
62	Post-traumatic brain atrophy	Collapse	Fractured skull
65	Chronic alcoholism	Fall	Fractured tibia and fibula
66	Delirium tremens	Fall	No summary
68	Acute alcoholism	Fall	Fractured skull, cerebral contusion
70	Osteoporosis	Fall	Compound fractured vertebra
71	Metastatic carcinoma of the lung	Fall	Pathologic fracture of the femur
80	Subarachnoid hemorrhage	Fall	Fractured ribs, contusion of the scalp

Fatalities during Hospitalization in Trauma Group. Table XI briefly describes deaths of patients occurring among the trauma group during hospitalization. There were nineteen such deaths in the 375 patients or 5.1 per cent of the sample. There were twelve deaths among 133 patients in the non-traumatic control sample and analysis shows significant difference in these mortality rates. The mean age at death of the patients who died was fifty-six ± seven years (traumatic) and fifty-two ± eight years (non-traumatic) demonstrating no significant difference between the mean age at death in the two groups.

Of the nineteen deaths of patients in the traumatic group, the cause of death was presumed in sixteen. Of these nine were due to the direct effects of the injury, six were due to secondary sepsis, and one was due to congestive heart failure for which no information is available as to the antemortem cardiovascular status of the patient.

Of all nineteen patients who died, four had reported concomitant disease. Of these four, two are indicated by † on Table XI; in these cases complete review of the record strongly suggests that the concomitant disease made the person prone to the development of the terminal situation. It is seen that of the six deaths of persons due to sepsis, five were patients over seventy years of age—in these five Staphylococcus aureus was the offending organism.

DISCUSSION

There are many limitations and weaknesses of this study. This series samples only those

TABLE XI

FATALITIES DURING HOSPITALIZATION AMONG TRAUMATICALLY INJURED PATIENTS*

Age (yr.) and Sex	Cause of Injury	Diagnoses	Day of Death in Hospital	Cause of Death
2, F	Automobile accident, fire	No summary	1	Burn shock
2, M	Hit by car	No summary	1	Multiple injuries
17, F	Automobile accident	Cerebral concussion and contusion	1	Cerebral trauma
18, M	Automobile accident	Bilateral subdural hematomas	2	Cerebral trauma
21, M	Automobile accident	No summary	1	?
37, M	Loss of consciousness	No summary	1	?
46, M	Automobile accident	No summary	39	Bronchopneumonia
48, M	Assaulted	Bilateral subdural hematomas, cerebral edema, intracranial hemorrhage	1	Cerebral trauma
71, M	Fall	Pathologic fracture of the femur, *metastatic carcinoma of the lung, coronary artery disease*	2	?
73, F	Hit by car	Retroperitoneal hemorrhage, ruptured viscus, compound fracture of the tibias and fibulas	18	Staphylococcic septicemia
73, F	Fall	No summary	4	Congestive heart failure
75, F	Loss of consciousness	Subdural hematoma, fractured radius, ulna	1	Questionable aspiration, pneumonia
77, M	Loss of consciousness	No summary	31	Multiple injuries
80, M	Hit by car	Fractured L1, pubis, femur, questionable renal trauma	3	Questionable multiple injuries
82, F	Fall	Fractured femoral neck, *chronic renal disease with uremia, arteriosclerotic heart disease with bundle branch block*	3	Questionable multiple injuries
†84, M	Fall	Fractured femur, *portal cirrhosis, arteriosclerotic cardiovascular disease, chronic lung disease*	16	Staphylococcic enteritis, pneumonia
84, F	Fall	No summary	36	Staphylococcic pneumonia
†86, M	Fall	Fractured femur, *diabetes mellitus, arteriosclerotic heart disease*	24	Generalized sepsis from wound
89, F	Fall	Fractured femur	32	Staphylococcic pneumonia

* Concomitant disease shown in italics.

† Clinically acceptable evidence of concomitant disease contributing to death.

traumatic admissions of people to the Emergency Ward and does not include those patients referred directly into the hospital. One is not justified in making generalizations describing other trauma populations on the basis of these observations alone. It is common knowledge among epidemiologists that one cannot determine whether a hospital population is representative of the geographical neighborhood in which the hospital is located. A person living in the police ambulance zone associated with this hospital may refuse admission to it and be taken to another one. Persons included in this study had to be ward or service patients, which therefore limited the range of income level from which such persons could come. In general, the study deals with only a low or lower-middle income group. The control group represents twelve admission days out of the year and although such a choice of days is

acceptable statistically, it is possible that the control group does not truly represent those admitted during the rest of the year.

The definition of acute trauma within two weeks of admission of the patients was arbitrary. Such a limit was chosen to make allowance for the person who hesitated to come to the hospital for some days after injury because he thought "it would all go away," as well as for the person who came to the emergency ward immediately. It was believed that injuries sustained earlier than two weeks before admission had a very great chance of being treated previously.

One can merely speculate about patients with inadequate histories. The presence of incomplete records is another weakness of the study. It was hoped that the weary house officer at 3 A.M., too tired to record everything he encountered, would be offset by the man on duty at 10 A.M., more fresh and alert. The surgical house officer who neglected to record all medical diagnoses would be similarly offset by the overscrupulous one who would record every minutiae of diagnosis.

Date on duration of hospitalization is significant only when comparing one age group's mean to another. The absolute duration of hospitalization may in certain instances reflect merely the type of management prevalent at a given hospital. The patients reviewed were managed and evaluated by different physicians and therefore the chances for uniformity in recording of histories, physical examinations and diagnoses were slim.

This study represents, it seems, the first of its type dealing with hospitalized patients and therefore there is no precedent for comparison. In the traumatic sample two facts seem clear. In general, the older the age group beyond twenty-nine years of age, the more women and the less men occurred, and the opposite was true for the younger age groups. Furthermore, it seems to have been the relatively large number of twenty to thirty-nine year old men and sixty years of age and older women that caused the significant age-sex differences in representation in the traumatic sample. The woman sixty years old or more who fell was an important figure in her age group. Of 124 persons aged sixty or more represented in the traumatic sample, 104 had fallen, and of these seventy-three were women and thirty-one were men. From all other causes of injury in this age group eleven men and nine women were encountered. In the non-traumatic group the older the age group beyond fifteen years of age the more males and the less females occurred, although these sex differences were not statistically significant. Falls were significant as causes of injury in this population. Fifty-seven per cent of all traumatic patients were injured because of falls. Even more striking is the fact that the group of patients aged sixty or more who had fallen composed 28 per cent of the entire traumatic sample.

Fifty-five per cent of all injuries were fractures, 48 per cent occurring in persons aged sixty or more. No other age-specific-injury trend of such proportions was encountered. Prevalence of concomitant disease is probably under-reported, since (1) only definite diagnoses were considered and (2) 32 per cent of traumatic patients (120 cases) had no discharge diagnoses indicated. The oldest age group had 11 per cent more patients with reported concomitant disease, the group forty to fifty-nine years of age had 7 per cent less and the group aged twenty to thirty-nine had 10 per cent less than would have been expected by chance, based on the overall rate for the three age groups of 72 per cent of patients without and 28 per cent with reported concomitant disease. By concomitant disease type, the group aged sixty or more produced the only two trends of any magnitude. It contributed thirty-six of thirty-eight diagnoses of cardiovascular disease and six of six diagnoses of genitourinary disease.

Of all traumatic patients, 9.2 per cent presented at admission concomitant disease requiring immediate recognition and treatment. Alcoholism, convulsive disorders and diabetes mellitus were the most frequent complicating conditions in that order. There was definite under-reporting of the contribution of concomitant disease to trauma production for two reasons: (1) the "possible contributory" concomitant diseases were not included in final consideration and (2) in certain instances, case histories hinted at a defect which could have contributed, yet was never diagnostically proved to be present or was never entered thereafter as a discharge diagnosis. In approximately 8 per cent (8.2 per cent) of the traumatic cases with summaries at discharge, injury was sustained because of the effects on the patient of pre-existing disease. In these twenty-

nine cases, alcoholism was the factor in eleven, epilepsy in seven, metastatic carcinoma in two, and nine were miscellaneous, one disease per case.

There were nineteen fatalities. Four patients had had concomitant disease, and of these, it was suggested that two (both of whom died of sepsis) were more liable to this terminal situation by virtue of concomitant disease also present. (Table XI.)

CONCLUSIONS

This study has demonstrated that the association of concomitant disease with the production and management of accidental trauma can be quantitated. Its practical implications can be used by the surgeons at the hospital in which the study was performed. The trends demonstrated may exist among other hospitalized populations also, and it is hoped that similar studies will be performed to investigate this possibility. If similar trends can be shown to exist in other geographical areas and populations, then a proper degree of emphasis can be placed by all physicians on considering concomitant disease as one factor in the subject of accidental trauma.

SUMMARY

The records of two groups of patients admitted to the wards of a large general hospital during a recent one-year period are reviewed and compared. One group of patients had been hospitalized for trauma, the other was admitted for all other reasons. The groups are described using various parameters. Special attention is given to concomitant disease both as a cause of trauma and as a complication in its management. Performance of similar studies throughout the United States is suggested, to investigate for trends of more than local significance and to add to the armamentarium for prevention of accidental trauma as well as to improve its over-all treatment.

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Automotive Crash Injuries to the Spinal and Femoral Linkages

A NEW BIOMECHANICAL POINT OF VIEW

JACOB KULOWSKI, M.D., *St. Joseph, Missouri*

COMPLEX multiple components of individual and variable parts of the problem of injury-producing automobile accidents are being clarified by clinical (mass statistical, epidemiological), laboratory, and full-scale crash methods of study. The ultimate aim of this prodigious effort is to achieve the best rider-vehicle combination. It seems appropriate to attempt reduction of cumulative data to larger more integrated concepts or common denominators. Since human elements are the keystone of the arch of preimpact, impact, and postimpact phenomena, bodily factors expressed in terms of basic engineering analogies may provide a start in this direction.

The purpose of this paper is to orient spinal, femoral, and related anatomy and physiology with this biomechanical concept. To begin with, data will be channeled and related to the link system of the body. Second, already existing physical defects of these major body linkages will be consolidated and categorized as "stress raisers."

An important result of this biological application of engineering principles was anticipated, i.e. the equivalence which exists between human engineering, crash-safety engineering and human salvage.* This means that all aspects of the clinical life history of motoring intersect and must be integrated to such an extent that one cannot be given pre-eminence or be dissociated from the other.

SOURCE OF MEDICAL DATA

Medical data on which this paper is based were extracted from two separate but essentially consecutive series of automotive crash patients. I saw one series of 250 cases in office orthopaedic practice from late 1947 until May 1957. All of these patients had residual complaints of varying duration after respective accidents referable to the spinal column, i.e. 40 per cent injuries to the neck, 40 per cent to the low back, and 20 per cent combined injuries to the neck and low back. The second series of crash cases was also selective in that only patients with acute skeletal injuries (fractures and dislocations) were included and consisted of persons who had been admitted to the Missouri Methodist Hospital during 1955 and 1956 (and were treated by members of the medical and dental staff, including myself). There were 175 patients with skeletal injuries totalling 252 fractures and dislocations.

LINK SYSTEM OF THE BODY

Dempster [1] has admirably described the human skeletal system in terms of mechanical linkages. In this case he reduced the twenty-four presacral vertebrae to three major links, i.e. the mobile cervical and lumbar which are connected by the stiffer thoracic link. The fraternal nature of spinal and femoral linkages is clinched by the triangular pelvic linkages which connect them. (Fig. 1.) The link is described by Dempster to be the straight line or core line which extends longitudinally through a body segment and terminates at both ends in axes or hinge points about which the adjacent members rotate. The various links may also be loaded by segment masses located at appropriate centers of gravity. Dempster stresses the difference between the closed machinery systems and the open ones of the human body. Machinery linkages are closed kinetic systems which assure

* "Whether or not a car causes injuries is not truly a definition of its safety. The purest definition of its safety is its likelihood or risk of being involved in an accident." (John O. Moore, 1956.)

that forces are transmitted in positive predetermined ways and in no other. However, the link in the human body is merely an abstract line which executes only those angular movements allowed by the joints related to it. Since the human linkages end in the head,

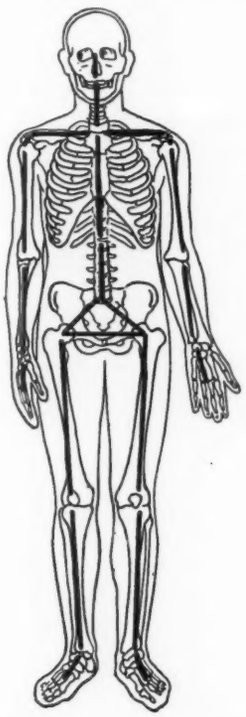


FIG. 1. Plan of body links, represented by heavy black lines. (From: DEMPSTER, W. T. The anthropometry of body action. *Ann. New York Acad. Sc.*, 63: 559, 1955.)

hands and feet the open kinetic system (which is rather indeterminate but also allows a greater freedom of action) predominates. If this were not so such actions as throwing a ball would not be possible. Also, the human being can close the kinetic system in various ways, i.e. by clasping the hands, pushing against something, tugging and pulling, crossing the legs, sitting, standing, etc. Where free movements of the end members occur the parts may be regarded as cantilever systems (Dempster), and the link span may be regarded as the straight-line distance from the terminal joint to the center of gravity of the part.

By the same token injuries may be interpreted from this viewpoint. Thus, the classic so-called whiplashing of the neck from rear-end collision represents an open chain reaction. When the head strikes something during that or any other maneuver the closed chain reaction operates. In that case the clinician is looking for even more severe evidences of injury to both the head and neck. With regard to the femoral linkages the knee-dash impact provides the most common example of closed chain injury. If instead the result is a dislocation at the hip joint (with or without concurrent acetabular or femoral fracture), by the same mechanism, this might be considered to be an open chain reaction for that particular injury. Apparently most of the residual spinal injuries derive from open chain mechanisms while acute skeletal injuries of the femoral linkages (including the upper tibia, patella, the knee joint, all parts of the femur, and the acetabulum plus adjacent elements) follow closed ones.

PHYSICAL DEFECTS AS STRESS RAISERS

Physical defects or deficiencies of the spine were noted and recorded in approximately 86 per cent (109 drivers, 106 guest passengers) of 250 patients with residual postcrash complaints.* Sixty per cent of those persons with disabilities of the neck after accident were complicated by arthritis of varying degrees. (Fig. 2.) In a large number of these the arthritis had been estimated to have been present prior to accident. In drivers in this category, the incidence of rear-end and angular collisions at intersections was significantly higher than in normal drivers. It is assumed that arthritis of the cervical spine may interfere enough with peripheral visual acuity to cause greater than chance rear-end and angular accident configurations.

As was also to be expected, all passengers with arthritis of the cervical spine seemed to be more vulnerable to crash injury, especially the so-called whiplashing variety. This is in accordance with the old adage that a chain is only as strong as its weakest link. In this case some of the weakness was probably due to interference with the spring-like action of the spinal segments (particularly since many of these patients showed variable pathologic condition of the disc in association with the arthritis).

The term stress raiser is applicable to all physical defects or deficiencies of this nature and others as well. Moore [2] defined these as

* Data referable to roentgen examination reports were supplied in all cases of both series by Drs. A. B. McGlothlan, Joseph L. Fisher, Randall Weed and Edsel Reed.

FIG. 2. Arthritis, the ubiquitous stress raiser epitomized in the frozen arthritic skeleton. (By courtesy of the Armed Forces Institute of Pathology. Acc. No. 23637. SILMORE and STECHER. *Mil. Med.*, 117: 432, 1955.)

causes of non-uniform stress conditions by surface discontinuities on the member, such as screw threads, shoulders, notches or some other form of inside corner. The same thing can apply to various general physical deficiencies, for example, diabetes, epilepsy, heart disease, etc.

With regard to femoral linkages, clues relating to causation of accidents are rooted in biomechanical requirements of the seated posture. This involves anterior rotation of the pelvis, compensatory flexion of the lumbar spine, plus considerable strength and coordination of the hip and adjacent musculature. (Fig. 3.) Clearly then, active vehicular occupancy achieves a labile not a static equilibrium. This is epitomized, of course, in the extraordinary instability of the body mass and masses of the unrestrained rider under crash conditions. Basically, during sitting under all conditions, the ability to pivot at the hips, both passively and actively, is a factor of safety of the highest magnitude.*

On the contrary, inability to pivot properly at the hips may result in severe injuries of the

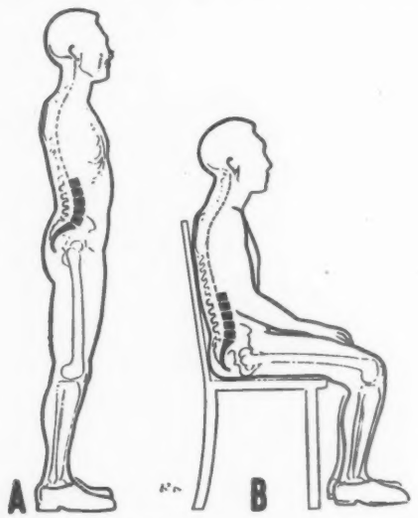


FIG. 3. Showing pelvic and lumbar changes from standing to sitting. (From: KEEGAN, J. J. Alterations of the lumbar curve related to posture and seating. *J. Bone & Joint Surg.*, 35A: 589, 1953.)

spine and/or atypical injuries of the femur (even though such inability might prevent head impacts on forward structures). There is considerable clinical evidence to support this premise. A good example (in my series) is that of a young man who received a severe crushing fracture at the dorsolumbar junction when the car in which he was riding in the back seat impacted a roadside embankment at an estimated speed of 40 to 50 miles per hour. Two men, one sitting on each side of him, escaped injury. There was little damage to the vehicle. The patient, however, had one ankylosed hip joint (surgically induced several years previously) which converted normal "jackknifing" to abnormal "flexion" at the hips and lower spine. Large flexion forces were responsible for the crushing injuries to this man's vertebral bodies.

Hugh De Haven has described a similar mechanism of injury which may result from an improperly worn safety belt during a forward

* The late great anthropologist, Dr. Earnest Albert Hooton, described the bony pelvis as the "pelvic wheel."

FIG. 4.

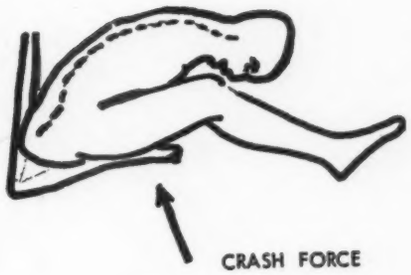


FIG. 5.

FIG. 4. Showing the differences between normal jackknifing and abnormal flexion. (From: DEHAVEN et al. Av-CIR report. Cornell University Medical College. July, 1953.)

FIG. 5. Showing factor of safety in ability to flex at the hips. (From: HASBROOK, A. H. et al. Av-CIR report. Cornell University Medical College. February, 1957.)

collision, i.e. when the belt is too high on the lower abdomen. This might conceivably cause an abdominal (wall or internal) injury. More likely, such improper use of the belt prevents normal pivoting at the hips with development of a high order of flexion forces which are transmitted to the spine. (Fig. 4.)*

The perfect corollary to the previously cited case of spinal fracture was recently reported by Hasbrook.† In this case two men escaped injury to their spines (which would have been expected from their estimated 50 g helicopter drop in which other severe injuries were received), by virtue of their ultimate flexion onto their thighs which changed the direction of the crash force from parallel to their spines to transverse. (Fig. 5.)

DYNAMIC BODY-LINK REACTIONS

The analogy to kinematic linkages was early appreciated by Edward Dye who extended this concept to his famed "Thin Man" and later "Thick Man" simulative crash experiments. His pioneering efforts yielded basic observations with regard to the kinematic behavior of the human body under crash conditions. More recently I presented him with the problem of the knee-dash impact. Mr. Dye was kind enough to work out the following answer. Based on his thin man impacting the instrument panel first and denting it 1 inch at an impact velocity of 10 miles per hour, assuming a man weighs 180 pounds the impact energy of the blow to the knees is between 40 and 60 per cent of the total energy of the body. Furthermore, assuming a perfect elastic deformation of the instrument panel, the maximum impact force on the knees would be in the neighborhood of 800 pounds. This agrees with laboratory loadings of the femur which frequently lead to tensile fractures.*

CLINICAL COMMENTS

The vast majority of injuries to the spine involve the soft parts, i.e. so-called sprains, often complicated by manifestations of injury to the nervous system. The spinal series of 250 patients comprised about 65 per cent of all patients with residual complaints of the motor skeletal (orthopedic) system seen during this interval of time. On the other hand a fair proportion of previous patients did show gross evidence of injury to the spine. This clinical variability is somewhat resolved when viewed from the standpoint of mechanism of injury (open versus closed kinetic chain), and the presence or absence of stress raisers. (Fig. 6.) The medicolegal implications are also considerable in view of the fact that more than 50 per cent of these people must be evaluated from this angle. This area of automobile injuries needs to be more fully explored, especially from the standpoint of possible complications of the central nervous system.

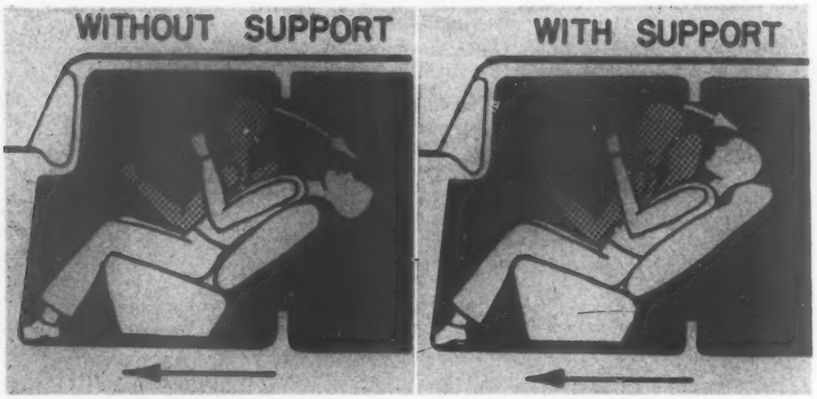
On the other hand, a study of the acute skeletal injuries, even on the basis of traditional clinical classification of trauma, yields a more objective picture. However, the body-linkage frame of reference is a more comprehensive one, albeit compressed. Classification according to body areas in the acute skeletal injuries is shown in Table 1.

From the standpoint of body linkages there

* DEHAVEN, H. et al., Av-CIR report, July 1953, New York City.

† HASBROOK, A. H. et al., Av-CIR report, February 1957, New York City.

* DYE, E. Cornell CIR reports. Buffalo, New York, 1950 and 1957. EVANS, F. G. Stress and Strain in Bones. Springfield, Ill., 1957. Charles C Thomas.



6A 6B

FIG. 6. A, typical first stage open chain reaction to rear-end collision. B, closing the chain in a prophylactic sense by extending the upper seat backward. (From: SEVERY, D. and MATHEWSON, J. Annual meeting of Society of Automotive Engineers, 1956.)

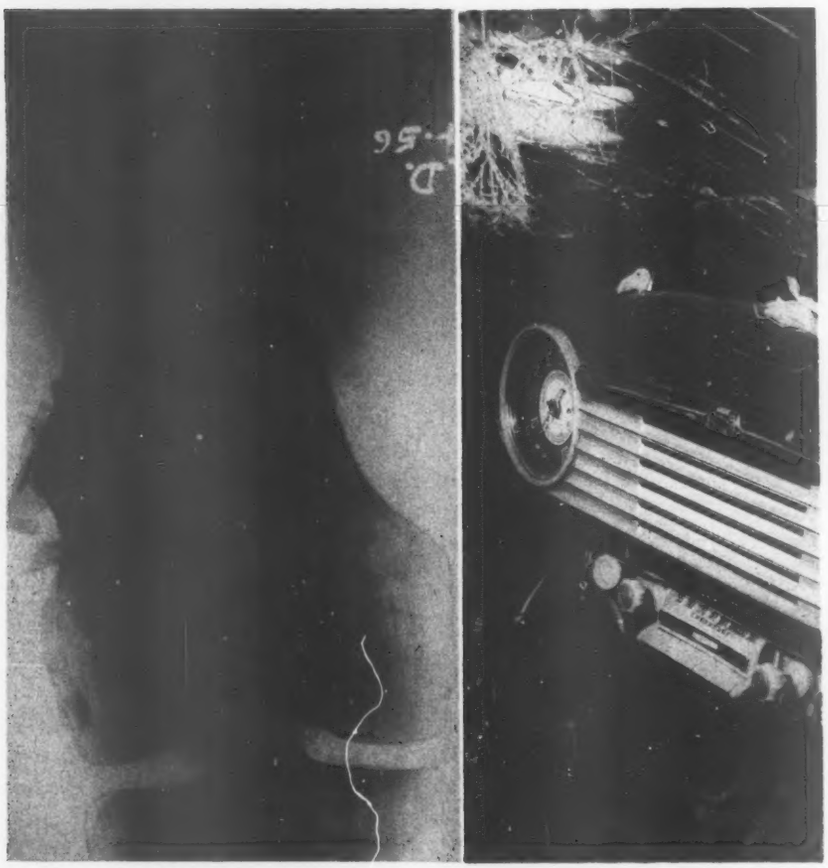


FIG. 7. Knee-dash impact (just to right of steering post) during forward collision with stress in an old-fashioned car, but the injury remains fashionable in modern vehicles.

were 11.5 per cent spinal injuries or about one-fourth of all injuries above the pelvic level. Also, almost 60 per cent of all injuries involving the lower extremities affected the femoral linkages (Fig. 7) (forty-one injuries in all including: injuries to the acetabulum, four; fracture dislocation of the hip, three; fracture of the neck of the femur, one; injury to the

trochanter, four; injuries to the upper third of shaft, one, to the middle third of shaft, twelve, to the lower third of shaft, one; injuries to the femoral condyles, three, to the patella, nine and to the tibial plateau, three).

TABLE 1

Body Area	No. of Injuries	Per cent
Head	12	4.76
Face	30	11.90
Neck	7	2.78
Chest	60	23.81
Dorsal spine	14	5.55
Lumbar spine	8	3.17
Pelvis	21	8.33
Upper extremity	48	19.02
Lower extremity	52	20.63
Total	252	100.00

CONCLUSIONS

Reduction of data may provide a more universal theory of accident causation, injury causation and human salvage in accordance with the principle of equivalence. From the standpoint of the vehicle this means that performance, operability and crash-safety must be integrated to the ultimate point of effectiveness. The apparent prevalence of stress raisers among a large segment of the motoring population gives special meaning to this statement.

For medical groups it spells the need for better control of the human variables involved (oddly enough engineers and others usually consider these to be a fixed and uncontrollable entity): first, through driver screening; second, by forewarning of impending danger from stress raisers under crash conditions; and third, by raising first aid, emergency care and definitive treatment to ever higher standards of acceptance.

The kind of biomechanical analysis introduced in this paper would seem to indicate that, at least in so far as the motor skeletal system is concerned, spinal linkages rank all other chronic disabilities, while the femoral ones are the most significant acute gross injuries. Undoubtedly, the buffer effects of chest impacts operate to spare the thoracic spine.

Finally, this biomechanical approach stresses common but non-lethal crash injuries which deserve more attention from epidemiologic, laboratory and full-scale crash investigators; these basic lessons are often blurred out in the volume of data which is being presented along traditional categorizations.

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Adrenal Tumors

PAUL J. CONNOLLY, M.D., WILLIAM S. CARPENTER, M.D. AND CHARLES G. JOHNSTON, M.D.,
Detroit, Michigan

RECENT advances in our knowledge of the function and dysfunction of the adrenal, from the stress syndrome through the discoveries of cortisone, hydrocortisone and aldosterone, have made the adrenal a subject of great interest. Clinical syndromes or mixtures of syndromes are being separated and ascribed to the hypo or hyperfunction of various components of the suprarenal gland. Knowledge of the symptom complexes which hyperfunction of the gland may produce increases our index of suspicion and the availability of functional tests or the assay or end-products may confirm these suspicions of adrenal tumors. With increased cognizance of the subject, we would expect the discovery of more of these tumors. With this in mind, we reviewed our cases as well as the subject in general and present the following paper.

Primary tumors of the adrenal may be derived from the supporting tissues or from the two glandular areas; the medullary cells and the cortical cells. We believe the following modification of Cahill's classification [2] to be a good working arrangement:

Stromal tumors (rare):

Fibroma	Neurofibroma	Sarcoma
Lipoma	Myoma	Lymphangioma
Neuroma	Osteoma	Melanoma
	Hemangioma	

Medullary cell tumors (from ectoderm):

- Sympathicoblastoma—from sympathetic nerve cell, extremely malignant
- Ganglioneuroma or neurocytoma—from sympathetic ganglion cell, benign or low grade malignancy
- Pheochromocytoma—from the pheochromocyte, a hormone cell, 91 per cent benign, 9 per cent malignant.

Cortical cell tumor (from mesoderm):

- Non-hormonal—benign or malignant
- Hormonal—benign or malignant:
  - Aldosterone producing cortical adenoma, causes primary aldosteronism
  - Adrenogenital, causes virilism
  - Adrenocorticoid, causes Cushing's syndrome
  - Mixed adrenogenital and adrenocorticoid

The non-hormonal group of tumors produce no signs or symptoms until they attain a size which is palpable. In the malignant group, metastasis may be discovered before the primary growth is palpable. At times these tumors are found incidentally during roentgenographic examinations, especially pyelography. Strong recommendations for removal should be made to patients who have these incidentally found tumors because of the danger of malignancy.

Much more interesting because of the varied clinical pictures they cause are the hormone producing tumors. The most recently recognized of this group are the functioning adrenal cortical adenomas. As described by Conn [4], the clinical picture is that of periodic, severe muscular weakness, intermittent tetany and paraesthesia, polyuria, and hypertension. The laboratory findings are abnormal in the blood serum and in the urine. The serum shows a low calcium with elevation of potassium, pH and carbon dioxide combining power (alkalosis). The urine has a low specific gravity which does not improve with pitressin,® is persistently alkaline and has a mild proteinuria. The diagnosis is established by high bioassays for urinary aldosterone. The condition is called primary aldosteronism. Cure may be obtained in two weeks by removal of a cortical adenoma, if present, or by adrenalectomy. We had one such case in our series.

Androgenic cortical cell tumors cause viri-

lism. Fortunately, since the diagnosis is more easily made in the female, the tumor occurs four times as often in the female as in the male. They produce a large clitoris, vaginal atrophy, increased pubic hair with the male distribution and increased musculoskeletal development. In such cases, arrhenoblastoma of the ovary should be ruled out and an investigation made for adrenal tumor. In the male, signs of puberty develop early without corresponding increase in the size of the testes. In these cases, bilateral adrenal hypertrophy may be differentiated from tumor by the use of cortisone. In hyperplasia, this will reduce the 17-ketosteroids in the urine but will not influence the urinary 17-ketosteroids in the patients with androgenic tumors. Most of these tumors are benign.

In patients with adrenocorticoid tumors Cushing's syndrome develops. The early changes are often difficult to detect but the fully developed syndrome is unmistakable. Cope and Raker [5] have listed twelve changes:

1. Obesity which is limited to the head, neck and trunk, with a puffed out, rounded, moon face, increased supraclavicular fat pads, a buffalo hump type fat pad between the shoulders and an obese trunk. The extremities are thin and wasted to a point where in spite of the obese appearance there may not be an over-all weight gain.

2. Skin changes consist of an atrophy of the entire body skin with prominently visible blood vessels. The face becomes florid and the extremities a blotchy marble color. Purple striae appear on the abdomen, hips, flanks, breasts and axillae. Acne is common.

3. Hirsutism may be helpful in the diagnosis in women. It is usually associated with recession of the temporal hair line.

4. Muscular wasting has been the most constant sign associated with the most common symptom, i.e., weakness and ease of fatigue.

5. Vascular fragility causes easy bruising.

6. Hypertension is present in 50 per cent of the patients.

7. Ankle edema is present.

8. Osteoporosis may cause a negative calcium balance and renal stones. Skeletal pain, especially backache, is present.

9. Gonadal suppression is not always present. Amenorrhea or irregularity in the female and impotence in the male may occur. Loss of libido may occur in both sexes.

10. Diabetes occurred in over 10 per cent in one series.

11. Mental difficulties such as irritability and inability to concentrate with brain atrophy may occur possibly due to loss of supporting tissues.

12. There is increased susceptibility to infections.

Hyperplasis of the adrenal cortex is a much more common cause of Cushing's syndrome than is neoplasm, but in either case the treatment of choice is surgery.

The only hormone producing tumor of the adrenal medulla, and, in fact, the only known condition producing hyperfunction of the adrenal medulla, is a pheochromocytoma. The adrenal medulla develops from ectoderm of the neural crest. Pheochromoblasts form pheochromocytes or chromaffin cells, so called because of the ability of the adrenal substances in them to reduce chromium salts to an insoluble peroxide of chromium which appears in the cytoplasm as fine brown granules. Ninety-one per cent of pheochromocytomas are benign.

In embryonal formation some of the pheochromocytes may migrate with the developing sympathetic ganglia to form paraganglia. The best known of these is the organ of Zuckerkandl situated at the origin of the inferior mesenteric artery from the aorta. Tumors in these extra adrenal areas are called paragangliomas.

Normally the adrenal medullary secretion is 14 to 20 per cent norepinephrine and the remainder is epinephrine. This order is reversed in pheochromocytomas to where norepinephrine may make up as high as 95 per cent of the secretion. A summary of the changes produced by these two substances is shown in the table on page 916.

It is thought that acetylcholine is the mediator of sympathetic and parasympathetic preganglionic nerve impulses and also of parasympathetic postganglionic impulses. Norepinephrine is thought [10] to be the mediator of postganglionic sympathetic impulses. Structures enervated by the sympathetic fibers respond to epinephrine but not necessarily with the same response as to nerve stimulation since this is mediated by norepinephrine.

Labbe in 1922 was the first to describe paroxysmal hypertension associated with pheochromocytoma [13]. Typically the attack consists of headache which is pulsating in nature,

pallor, numbness and sweating. There may be a surging sensation in the chest, epigastric pain and sometimes vomiting, breathlessness, dizziness, anxiety, tremulousness of the extremities and intolerance to heat. Extreme weakness may follow the attack. In some cases there

Data	Epinephrine	Norepinephrine
Cardiac output	Strikingly increased	Slight increase or decrease
Systolic blood pressure	Significant rise	Significant rise
Diastolic blood pressure	No change to slight drop	Significant rise
Mean blood pressure	Slight rise	Significant rise
Pulse rate	Increased	Decrease
Peripheral resistance	Decreased	Striking increase
Emotional state	Increased	Unchanged
Glycogen breakdown	Much increased	Slightly increased

may be acute cerebrovascular disturbances (encephalopathy) with quick recovery free of residue. Dilation of the pupils and glycosuria may be found with elevated blood pressure.

The attacks may be precipitated by changes in position, change in temperature, emotional stress, hyperventilation, physical exertion, operative procedures, massage or blows to the abdomen, pain, or by activities such as gargling, sneezing, sexual intercourse or bowel movements [*9,10,21*]. The attacks may last for a few minutes up to several days.

This dramatic symptom complex suggests pheochromocytoma. Less obvious is the diagnosis in the patient with persistent hypertension. Smithwick, while performing sympathectomies for hypertension, explored the adrenal areas and found an incidence of pheochromocytomas of 0.5 per cent. Green found 70 per cent of fifty-one patients with pheochromocytomas to have persistent hypertension. Even in patients with persistent hypertension there may be paroxysmal attacks with some of the above listed symptoms. Some helpful points in suggesting a diagnosis in patients with sustained hypertension are: (1) normal cold pressor response, (2) persistent tachycardia, (3) basal metabolic rate over plus 20 per cent, (4) fasting blood sugar over 140 mg./100 cc., (5) glycosuria, (6) postural hypertension, (7) hypertension under fifty years of age, (8) associated neurofibromatosis (occurs in 5 per cent), (9) palpable flank tumor, and (10) elevation of blood pressure above resting state by flank massage.

To establish a diagnosis the determination of the amounts of epinephrine and norepinephrine circulating in the patient's blood stream, especially during an attack will be conclusive. These tests are time consuming and difficult to perform and therefore expensive and not suitable for screening. Several colorimetric and paper chromatographic tests for pressor amines are being studied, and possibly a desirable test will be found. A biological test with no false negative or positive results in seven cases of pheochromocytoma out of 250 hypertensive patients tested has been reported by Moulton [*16*]. This test consists of injecting urine, untreated except for the addition of vitamin C to prevent oxidation, into the femoral vein of cats, and comparing the animal's blood pressure response with that of known amounts of epinephrine.

Pharmacological tests for pheochromocytoma are divided into two groups, the provocative and the adrenergic blocking tests. Histamine, mecholyl bromide, dimethyl 4 phenylpiperozinium, tetraethylammonium bromide and methacholine chloride are all provocative agents. The exact mechanism by which they produce attacks is not known. Histamine is the safest and most reliable of this group. In performing any provocative test, adrenergic blocking agents should be ready to prevent severe or even fatal attacks. The histamine test should be used in patients with paroxysmal hypertension in whom the pressure is lower than 170/110 mm. Hg. This consists [*17*] of the intravenous injection of 0.025 to 0.05 mg. of histamine base in saline solution, using the smaller dose first. The patient should be in the recumbent position before the test is given until the blood pressure is steady. Blood pressure is recorded every minute for five minutes and in a normal person will rise 5 to 10 mm. Hg. If a pheochromocytoma is present, the blood pressure may rise 100 mm. Hg, and a typical symptomatic attack may be provoked. A positive test is one in which the blood pres-

sure rises 60/30 mm. Hg or more and remains elevated for five to fifteen plus minutes or in which the rise is appreciably above that of the cold pressor test.

During the hypertensive stage, the adrenergic blocking substances are used as testing agents:

1. They are regitine,® rogitine, phentalamine, or 2-(N, para-tolyl-N, M-hydroxylphenol aminomethyl) imidazoline hydrochloride. With the patient in the recumbent position, intravenous fluids are started and the blood pressure checked until stable. Five to 10 mg. of regitine is then given intravenously. A drop of 35/25 mg. Hg or more is considered positive for pheochromocytoma. A false positive response will occur if the patient has received sedation or hypotensive drugs in the preceding forty-eight hours, if the patient is uremic or if large amounts of regitine are used.

2. Benzodioxane, benodaine® piperoxan or piperidylmethyl benzodioxane. The majority of hypertensive patients have a moderate pressor response to this drug while most patients with pheochromocytoma have a drop in blood pressure. Some patients with pheochromocytoma will have an initial hypotensive response followed by a marked pressor response and this is especially true if the test is made while the patient is normotensive. Some false negative and false positive results have been reported, and side effects are common and undesirable such as tachycardia, flushing, palpitation, headache, dizziness, and in the patient with essential hypertension, pulmonary edema and encephalopathy.

It has recently been found that benzodioxane produces an antidiuretic response in patients with pheochromocytoma [*14*]. Accordingly, the test has been modified so that the fasting, recumbent patient is given 1 L. of 0.25 per cent solution of saline orally, and urine is collected for three or four successive thirty-minute periods. Benzodioxane is given intravenously after the second collection period and its effect on blood pressure noted during the third collection period. In patients with pheochromocytoma the volume of the third urine sample is substantially reduced while in controls there appeared a diuretic effect, and the third urine sample was greater in volume.

3. The action of dibenamine or dibenzyl-B-chlorethylamine hydrochloride lasts twenty-four to seventy-two hours. It also causes a drop in blood pressure in essential hypertension [*22*], and has toxic side effects.

None of these tests are completely satisfactory because of false positive tests, and because as Goldenberg has shown, "prolonged hypertension due to pressor amines may lead to arteriolar damage and persistent essential hypertension which is not affected by adrenolytic agents, and which will give rise to false negative tests."

Clinical examination may reveal a palpable tumor, or massage in one kidney area may produce an attack giving indirect evidence of the location of the tumor. Since 10 per cent of these tumors are bilaterally in the adrenals, and 8 per cent in paragangliomas [*15*], some surgeons do not believe it essential to localize the tumor. If the pheochromocytoma can be localized, however, it simplifies the choice of operative approach.

Incidentally, in the six reported cases of familial pheochromocytoma, five have been bilateral, and in the sixth, only one side was explored [*11*].

A plain film of the abdomen may show a soft tumor, or pyelograms may show a kidney depressed by tumor. Tomograms or laminographic x-ray studies may facilitate localization. Presacral oxygen injection, while not without danger, has well demonstrated the tumors reported in this study.

While steroids may be used in preparing patients for operation, this has been objected to on the basis that water and salt retention would render the hypertensive state seen during the manipulation of the tumor more hazardous [*3*]. If bilateral tumors are found or suspected, then cortisone or hydrocortisone is indicated preoperatively. There is also some danger in using atropine for preoperative medication since it potentiates the pressor response to noradrenaline and increases the tachycardia [*8*]. This may be prevented by giving regitine before the preoperative medication. Since curare has a histamine-like action, it should not be used as an anesthetic agent.

There are three stages of danger during the operative procedure. The first is the danger of producing a paroxysmal attack during the positioning of the patient or the induction of anesthesia. The second is the hypertension which may be produced during the manipulation of the tumor in examining or removing the tumor. The third stage follows the removal of

the tumor when profound hypotension may occur. These dangers are prepared for by having a solution of 5 per cent glucose in water (saline is contraindicated by the danger of pulmonary edema) running into a vein and with a syringe filled with noradrenaline, and another syringe filled with an adrenergic blocking agent (regitine) ready to be given through the intravenous tubing as needed to keep the blood pressure steady.

During the six-year period, 1950 through 1955, a total of twenty-five cases of tumor of the adrenals, and two cases of paraganglioma, were discovered at Detroit Receiving Hospital. In addition, two cases from our private practice are added, making a total of twenty-nine cases. The largest group, thirteen cases, consisted of the incidentally found cortical adenomas. There was one case of functioning cortical adenoma with primary aldosteronism and one hormone producing carcinoma of the cortex with the adrenocorticoid syndrome. The adrenogenital syndrome was found in two additional patients in whom tumors were not proved and these two patients were not operated upon.

The second largest group of tumors were pheochromocytomas. There were eleven such tumors. Of these, three patients were operated upon and cured of their hypertension. A fourth patient with congenital heart disease died of cardiac arrest as the skin incision was made. A fifth patient was admitted with severe focal necrosis of the liver. This patient died after a biopsy of the liver and biopsy of a large pheochromocytoma were performed under local anesthesia. The operation was performed in this extremely ill patient because of acute abdominal distention, absence of bowel sounds, and an enlarging mass in the right upper quadrant of the abdomen. A sixth patient became maniacal, went into shock and died following an aortagram. At autopsy, she was found to have hemorrhage into the right adrenal. This, to our knowledge, is the third reported case of death following aortography in patients with pheochromocytoma [12,19]. In all three cases death was due to hemorrhage in the area of the tumor and was not associated with the needle puncture. This, we believe, is sufficient to condemn aortography as a diagnostic method in patients suspected of having this tumor. The remaining five patients were admitted in coma or in a terminal state. In only one of these cases was there an opportunity for diagnostic tests, and the presence of pheochromocytoma was established in most of them at the autopsy table. These five cases and the patient with focal necrosis of the liver are of interest from the standpoint of what might have been done for them had an earlier diagnosis been established. Three died of cerebrovascular accidents, two of cardiac failure, and the last of focal necrosis of the liver, associated with hypertensive cardiovascular disease. Had the presence of pheochromocytoma been known before the terminal episodes, surgery might have lowered the hypertension and prolonged their lives. It must be pointed out, however, that these patients all entered a large city hospital and were not the type of patient who seek early medical care.

There were three tumors of stromal origin. There was one myelolipoma, one neurofibroma and one fibroma. All were incidental autopsy findings.

There were nine cases of metastasis to the adrenals which are not included in this series of primary tumors. They are mentioned only to suggest that adrenal hypofunction may be a cause of death in carcinomatosis, or, on the other hand, it may explain the reported spontaneous regression of carcinoma of the breast in a few patients. It is possible that metastasis produces a functional adrenalectomy which might cause regression of a hormone dependant tumor.

CASE REPORTS

CASE I. R. G., a thirty-four year old Negro woman, was admitted to Detroit Receiving Hospital, with the complaints of muscle cramping and weakness. She was principally upset by a "drawing up" of her hands. Physical examination showed only two abnormalities; a blood pressure of 180/110 mm. Hg and a positive Trousseau's sign. Repeated laboratory tests showed the following ranges: sodium 147–155, potassium 1.8–2.6, calcium 9.1–10, phosphorous 2.3–3.4, and carbon dioxide combining power 58–78. Clinical diagnosis was primary aldosteronism.

Air insufflation studies showed a suspiciously large left adrenal. This area was explored and a globus tumor found on the posterior lateral surface. A total left adrenalectomy produced a return to normal of the blood chemistries and a disappearance of the patient's symptoms.

CASE II. M. B., an eight year old Negro boy was admitted to Detroit Receiving Hospital, with

a one-year history of loss of weight in spite of a ravishing appetite. For the past month he had impairment of vision, severe occipital headaches, night sweats, projectile vomiting, urinary frequency, palpitation and periorbital edema.

Physical examination revealed a lethargic Negro male child with puffy eyes. Blood pressure was 210/160 mm. Hg. The fundi showed papilledema, grade 1 on the left, and grade 3 on the right, with cotton wool exudate and hemorrhage with marked niching of the arterioles and spasm and constriction of grade 4. There was a small mass palpable medial to the left kidney. Massage in the left kidney area caused a rise in blood pressure. Intravenous and retrograde pyelograms were made and there was found to be rotation of the left kidney pelvis with localized lateral displacement of the left ureter below the kidney pelvis. Benzodioxane test was positive. A preoperative diagnosis of paraganglioma near the left renal artery was made and the patient taken to surgery. The abdomen was opened by a left transverse incision and a firm tumor found medial and anterior to the lower pole of the left kidney. The right adrenal was normal and the left was small. The blood pressure rose on manipulation of the tumor. The tumor was removed but an opening was made in the left renal vein. This was closed by suturing. Pathologically, the tumor was a paraganglioma. (Fig. 1.) It was necessary to readmit the patient to the hospital for a left nephrectomy because of complete infarction of the left kidney. The patient was seen five years later with normal fundi and a blood pressure of 130/100 mm. Hg.

FIG. 1. Pheochromocytoma removed from eight year old boy with hypertension.

CASE III. L. G., a thirty-one year old Mexican woman was admitted to Detroit Receiving Hospital, with a history of profuse perspiration and progressive weakness and fatigability for one year's duration. She had noticed increased irritability and emotional instability. She also had episodes of palpitation associated with prickling precordial pain and dyspnea. This occurred especially with emotional distress. She had a poor appetite and had lost 10 pounds in the last two months. Examination disclosed a blood pressure of 170/115 mm. Hg. There was a pea-sized nodule in the left lobe of the thyroid. There was a questionable mass in the right upper quadrant of the abdomen. A preadmitting basal metabolic rate was plus 90, and when repeated, with the patient under sedation with 3 gr. of nembutal,® it was plus 92. Cholesterol levels and protein-bound iodine were normal. Intravenous and retrograde pyelograms were normal. Regitine produced a drop in blood pressure. Histamine given at a time when the pressure was 130/80 mm. Hg produced an immediate fall to 80/40 mm. Hg with a slow climb back to 150/100 mm. Hg.

The patient was explored transabdominally, and a 4 by 4 by 3 cm. tumor was found in the region of the right adrenal. Manipulation of the tumor caused an increase in blood pressure. Following the removal of the tumor, which microscopically was a pheochromocytoma, the patient made an uneventful recovery and was discharged from the hospital with a normal blood pressure.

CASE IV. R. P., a thirty-one year old white man was admitted to Harper Hospital because of hypertension of one year's duration. The hypertension was discovered during a routine physical examination. Aside from frequent nervousness, he felt perfectly well.

Physical examination revealed a single abnormality, a blood pressure of 220/120 mg. Hg. A regitine test was negative, benodane test was equivocal and the histamine test showed a rise which was not diagnostically significant. Excretory urograms showed a displacement of the right kidney downward with slight rotation, suggesting a mass in the region of the suprarenal. Presacral oxygen insufflation demonstrated a round soft tissue mass of added density between the upper pole of the right kidney and the diaphragm. (Fig. 2.) Through a thoracoabdominal incision, a 13.5 by 8.5 by 6 cm. encapsulated tumor was removed from the right adrenal region. (Figs. 3 and 4.) Microscopically this was a pheochromocytoma. The patient made an uneventful recovery, except for a flare-up of malaria which he had suffered previously. He left the hospital on the eleventh

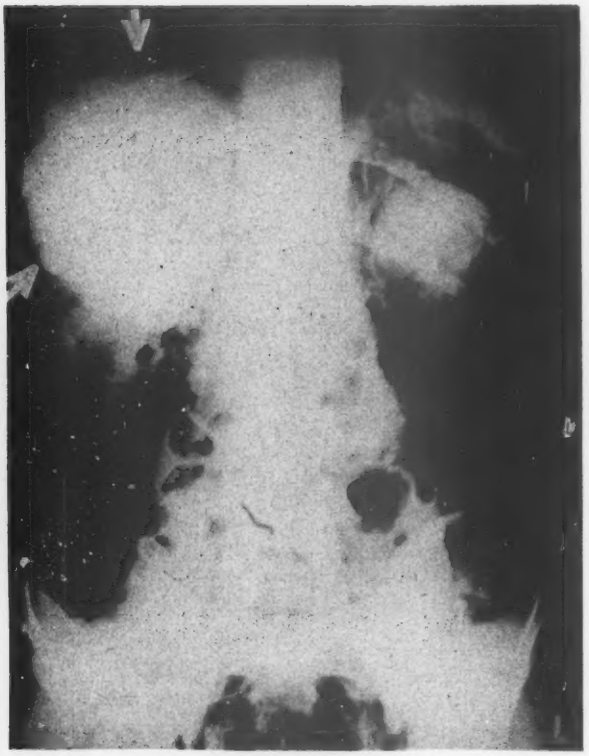

FIG. 2. Presacral oxygen insufflation showing large mass in right renal area in Case IV.

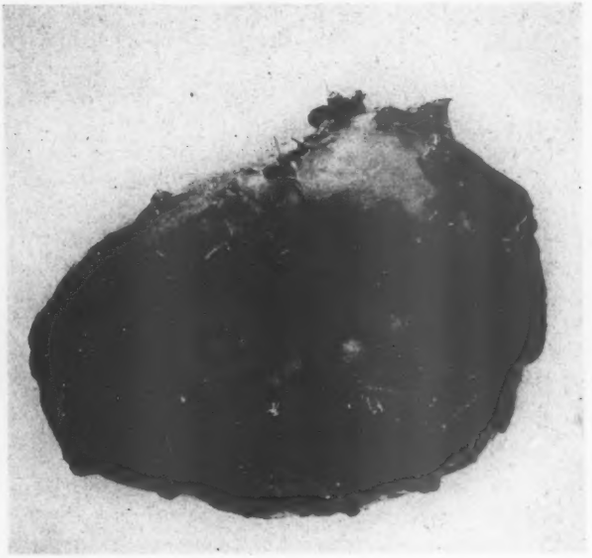

FIG. 3. Pheochromocytoma removed in Case IV.

FIG. 4. Bisected pheochromocytoma of Case IV.

postoperative day with a blood pressure of 120/80 mm. Hg.

CASE V. J. L., a twenty-nine year old white man entered Sinai Hospital because of migrating aches and pains all over the body for three months. In addition, he had weakness of all extremities with tingling of the hands and feet. Three months previously, polyuria with nocturia, polydypsia and polyphagia had developed. His appetite was such that even though his stomach felt full he was not satiated. He had gained twenty-five pounds in the last year but had lost some of this since being placed on a diet. His cheeks became puffy and purple lines appeared on his legs and abdomen. Blurring of vision had been present for the last two months, associated with right frontal headaches. Both his mother and grandmother had diabetes.

Physical examination disclosed a white man with rounded cheeks and face, and a buffalo-type obesity. The skin of the head, face and neck were a reddish tan color. There was paralysis of upward gaze in the right eye. There were purple striae on the abdomen, thighs and legs. In the left subcostal area, a mass could be felt one and a half inches below the costal margin on expiration, which on inspiration became a large firm mass.

Significant laboratory findings were a fasting blood sugar of 76, an eosinophil count of 83.2 per cu. mm., and a 17-ketersteroids excretion of 29.9 mg. per twenty-four hour specimen.

An excretory urogram showed duplication of the right upper urinary tract involving calcyces, pelves and ureters. On the left, the renal pelvis and calyces were somewhat low in position as compared to the total renal outline. Presacral oxygen insufflation

FIG. 5. Presacral oxygen insufflation showing large tumor mass in left renal area in Case v.

planigraphy of the left suprarenal area showed a large tumor mass. (Fig. 5.)

The patient was prepared for surgery with 50 mg. of cortisone, orally, every six hours, for twenty-four hours, preoperatively, and an additional 100 mg., intramuscularly, before operation. He was operated through the bed of the subperiosteally removed twelfth rib. A 12 by 11 by 8 cm. tumor was removed along with a segment of apparently normal adrenal. The wound was closed about a rubber drain.

Following the operation, the patient was given 50 mg. of cortisone every four hours, desoxycorticosterone 5 mg. and acthar* gel 80 mg. The DOCA, cortisone and ACTH were reduced daily. DOCA and cortisone were discontinued on the fifth postoperative day, and the ACTH on the ninth day after operation. Additional salt was given orally as soon as the patient began to eat. By the sixth postoperative day, the striae were disappearing and the facial flush was lessening. The patient left the hospital on the eleventh postoperative day.

Microscopically, the tumor was a carcinoma of the cortex of the adrenal gland. (Fig. 6.)

The patient did well for six weeks when pain developed in the mid-abdomen, and in the operative site. His course was then steadily downhill with the development of ascites, chest metastasis and a mass in the left flank. Urinary ketosteroids began to rise and reached a high of 63.7 mg. per twenty-four hour specimen. X-ray treatments were given without improvement and the patient died four and a half months after operation.

FIG. 6. Photomicrograph of carcinoma of adrenal cortex in Case v illustrating irregular columns, cords and nests of neoplastic cells.

SUMMARY

Adrenal tumors may be divided into three groups, stromal, medullary and cortical. All adrenal tumors should be removed as soon as they are discovered because of the danger of malignancy.

The non-hormonal tumors produce no signs or symptoms until a palpable mass is found. In the malignant group, metastasis may be discovered before the primary tumor is palpable.

The hormone-producing tumors are from the medullary portion of the adrenal or from the cortical. The only medullary hormone producing tumor is the pheochromocytoma which causes an increase in the pressor amines. Clinically, this is evidenced by hypertension, either sustained or paroxysmal. The diagnosis is incontrovertible when the pressor amines are found in excess but the tests are difficult. Screening tests are helpful but not infallible. The best of these tests are the histamine provocative test in the normotensive patient, and the regitine adrenergic blocking test in the hypertensive patient. Presacral oxygen insufflation and intravenous pyelograms may localize the tumor. Aortography should not be performed. If localization is not possible, the patient should be explored transabdominally

and in addition to exploring the suprarenal areas, paragangliomas should be looked for along the sympathetic ganglia. Since hypertension, due to this tumor, is almost always cured by the removal of the tumor, physicians should be alert to detect this growth.

Cortical hormonal tumors may produce either of three clinical pictures: (1) Primary aldosteronism is characterized by periodic severe muscular weakness, intermittent tetany and paresthesia, polyuria, polydipsia and hypertension. Elevated urinary aldosterone establishes the diagnosis although other findings are characteristic, such as low serum calcium with elevated potassium, pH and carbon dioxide combining power. (2) Androgenic cortical cell tumors cause virilism. Fortunately, since the diagnosis is more easily made in the female, the tumor occurs four times as often in the female as in the male. (3) Adrenocorticoid tumors produce Cushing's syndrome. The surgical removal of cortical tumors produces cures in the non-malignant cases and in the malignant cases when cortical tumors can be totally removed before metastasis has taken place.

A series of twenty-nine tumors of the adrenals, discovered in a period of six years, is reported. Reports are given of five cases in which surgery was performed.

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Papillary Cystadenoma Lymphomatosum (Adenolymphoma)

A REVIEW OF THE LITERATURE

A. P. CHAUDHRY, B.D.S., M.S., PH.D. AND ROBERT J. GORLIN, D.D.S., M.S., *Minneapolis, Minnesota*

From the Division of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis, Minnesota.

PAPILLARY cystadenoma lymphomatosum is a benign neoplastic disease of the major salivary glands. It affects chiefly males between forty and seventy years of age and is characterized clinically by a well defined round or ovoid swelling either in the parotid gland or in the periparotid regions. Histologically it is composed of epithelial papillary processes projecting into dilated cystic spaces. These processes are supported by lymphoid stroma containing germinal centers.

The neoplasm was first reported in 1895 by Hildebrand [*50*], who considered it one of the variants of lateral congenital cysts of the neck. It was not until 1910 that Albrecht and Arzt [*2*] described it as a separate entity and called it papillary cystadenoma in a lymph node. In 1923 Nicholson [*82*] reported the first English cases, describing the tumors as adenomas of heterotopic salivary glands in the preparotid lymph nodes. In 1929 Warthin [*118*] in this country reported two cases of this tumor from a collection of 700 cases of mixed tumors of the parotid and over 500 branchial cysts of the cervical region. He designated it papillary cystadenoma lymphomatosum. In 1935 Carmichael, Davie and Stewart [*17*] reviewed twenty-six previously reported cases and added eight of their own. In 1942 Plaut [*92*] collected forty-eight cases from the literature, to which he added sixteen new cases. The largest group of twenty-two cases was contributed by Martin [*72*] in 1944 from the Cancer Memorial Hospital, New York City. However, some of these cases were included in Plaut's publication. In 1950 Thompson and Bryant [*112*] studied extensively the histogenesis of papillary cystadenoma lymphomatosum and added seventeen new cases to 163 previously reported. In 1956 Orloff [*87a*] presented a detailed review of the clinical and pathological characteristics of 291 cases of papillary cystadenoma lymphomatosum gathered from the world literature. The present authors conducted an independent survey of both the domestic and foreign literature available and have been able to collect 349 cases of this neoplasm and have also added eight new cases from the files of the University Hospital and Mount Sinai Hospital, Minneapolis, bringing the total to 357 authentic cases. The clinical findings in eight new cases have been summarized in Table 1. This survey does not include controversial cases* nor those authentic cases published in the literature unavailable to us.

The neoplasm has been referred to by several different names.† The most commonly

* Controversial cases: Lederman (Case 1), Nicholson (Case 1), Heinz (case arising from vocal cords), Berner (Case 5), Delanglade et al., Lücke, Morestin, Sultan, Gödel, Hanford and Ssobolew.

† Synonyms for this neoplasm are: congenital epithelial cyst of the neck [*50*]; branchial cyst of the parotid [*20*]; cystadenoma of the parotid [*63*]; papillary cystadenoma in lymph node [*2*]; papillary intralymphnodular cystadenoma [*37*]; branchiogenic adenoma of neck [*41*]; branchiogenic papillary cystadenolymphoma [*32*]; branchioma [*107*]; epitheliolymphoid tumor of parotid [*23*]; lymphoglandular cystoma [*84*]; papillary cystadenoma with lymphoid supporting tissue [*24*]; cystic papillary adenoma [*82*]; papillary cystadenolymphoma [*73*]; kyste amygdaloide [*76*]; tumeur amygdaloide [*47*]—polykystiques; cystadenolymphoma parotids [*108*]; adenoma branchiogenes cylindrocellulare cystium [*3*]; papillary cystadenoma lymphomatosum [*118*]; papillary cystadenoma [*11*]; onkocytoma [*53*]; orbital inclusion cyst [*59*]; adenolymphoma [*38*]; adenocysticum lymphomatosum [*41*]; Warthin's tumor [*72*].

TABLE I
SUMMARY OF CLINICAL FINDINGS IN EIGHT NEW CASES

Case, Age (yr.) and Sex	Location	Side	Size (cm.)	Duration (mo.)	Follow-up
I, 74, M	Parotid	Right	4 × 3.5 × 2	3	No recurrence for 6 mo.
II, 63, M	Parotid	Right	7.5 × 6	24	No recurrence for 2 yr.
III, 62, M	Parotid	Left	4 × 2.5 × 2	6	No recurrence for 3 yr.
IV, 70, M	Parotid	Left	2.5 × 2.5 × 2.5	6	No recurrence for 5 yr.
V, 60, M	Parotid	Left	.....	3	No recurrence for 3 yr.
VI, 50, M	Parotid	Left	5 × 4	36	No follow up
VII, 47, F	Parotid	Right	2 × 1.8 × 1.4	..	No recurrence for 18 mo.
VIII, 59, M	Parotid	Left	1.5 ×1.5 × 1.5	2	No recurrence for 3 mo.

used are: adenolymphoma (Hall), onkocytoma (Jaffé), Warthin's tumor (Martin) and papillary cystadenoma lymphomatosum (Warthin). The name adenolymphoma, extensively used in Europe, is concise and descriptive of the histologic components of this tumor but it exaggerates the importance of lymphoid tissue at the expense of the epithelial tissue which constitutes its prominent feature. Jaffé [*53*] proposed the term onkocytoma for this tumor, attributing its origin to large oxyphilic granular cells, called onkocytes by Hamperl [*39*] and pyknocytes by Zimmermann [*124*]. This name has not been well received since there is no convincing proof that the neoplasm arises from onkocytes. Since Warthin [*118*] is credited with the first reported cases in America, the term Warthin's tumor has been commonly employed for this neoplasm for sake of simplicity. The term papillary cystadenoma lymphomatosum, although long and cumbersome, has been widely accepted by most of the pathologists since it describes appropriately the histological components of the lesion.

The papillary cystadenoma lymphomatosum is reported to comprise 2 to 6 per cent of all parotid tumors and from 1.6 to 4.2 per cent of all new growths of the salivary glands [*87*]. In a review of 120 cases of salivary gland tumors at University Hospital the authors encountered six cases of papillary cystadenoma lymphomatosum, constituting 5 per cent of all salivary neoplasms. Of 242 cases among 349 in which age was specified, 82 per cent were between forty-one and seventy years of age, the majority being in their 6th decade. (Fig. 1.) The youngest patient was two and a half years of age and the oldest was ninety-two, with an average age of 55.6 years. Of the 306 cases in which sex was listed, 257 were males and

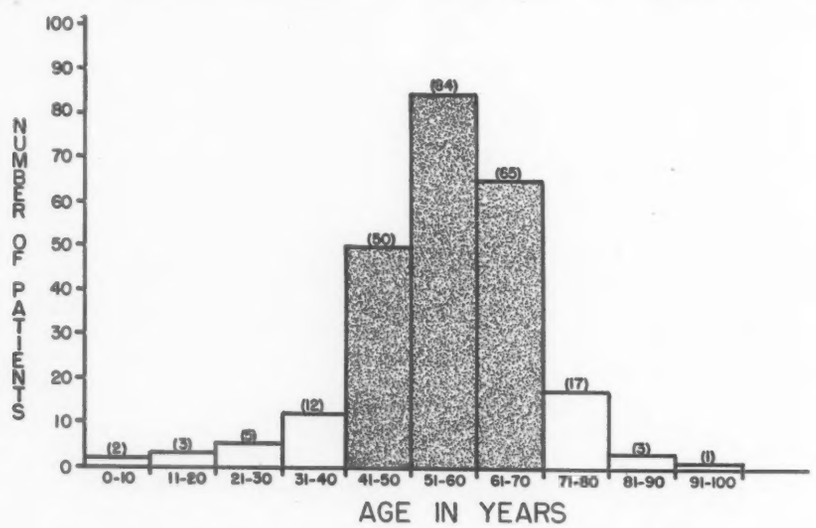

FIG. 1. Age distribution of papillary cystadenoma lymphomatosum.

forty-nine females, constituting a male to female ratio of approximately 5:1. (Fig. 2.) Four cases have been recorded in Japanese people [8,79,81,86], three in Egyptians [4], one in an East Indian [35], and one in an African Negro [27]. The tumor occurs primarily in white people since no case has been reported in an American Negro. The neoplasm is exclusively limited to the parotid glands or the periparotid region. Before Martin's review of the subject six cases were reported to have occurred in the submaxillary gland. Due to the close proximity of the inferior portion of the parotid gland to the posterior part of the submaxillary gland, Martin suggested that these cases were also of parotid origin. This concept has been very well accepted by subsequent investigators and no case has been reported to have arisen from the maxillary gland thereafter. However, one case has been reported to have occurred in the hypopharynx [46]. This has been believed to be an extension from the parotid gland since the entire growth was not visualized. The authenticity of another case, which seemed to have originated from the false vocal cords [43], has also been challenged as true papillary cystadenoma lymphomatosum. Thus it is the consensus of pathologists that this neoplasm originates exclusively from the parotid gland or its immediate environs. The neoplasm may be located in any part of the parotid gland. However, most commonly it is found next to the angle of the mandible involving the lower pole. The second most common location is in front of the lobule of the ear. The neoplasm may lie superficial or deep to the parotid fascia or actually in the substance of the gland or, occasionally, posterior to it. Of the 210 cases in which location was stated, 101 involved the right parotid and 95 involved the left parotid; in fourteen cases there was bilateral involvement. Thus the neoplasm is almost equally distributed on the two sides. In seven patients the tumor was multicentric in origin. In three instances it was associated with primary tuberculosis [19, 88,96], in two with malignant lymphoma [72,97], and in one case with mucoepidermoid tumor [81]. Of the 182 cases in which duration was specified 40 per cent of the patients consulted a physician within one year of the onset of the disease. This short duration could be attributed to the apparent facial asymmetry caused by the tumor when superficially located. The shortest duration reported was two weeks and the longest thirty years, with an average duration of thirty-six months. In 160 cases there was information concerning the size of the tumor mass. The largest tumor was 8.5 cm. long and the smallest 1 cm., with an average

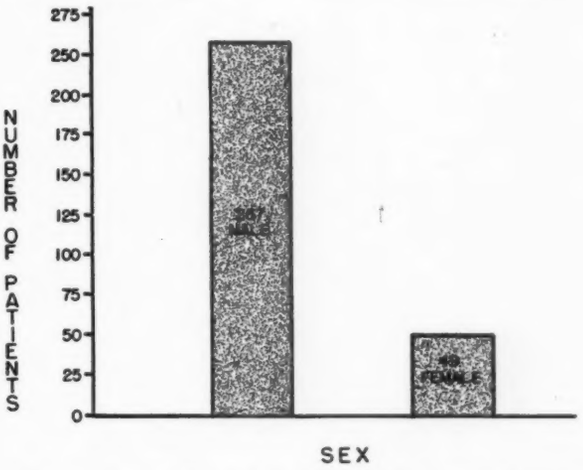

FIG. 2. Sex distribution of papillary cystadenoma lymphomatosum.

length of 3.6 cm. There was gradual increase in size of the tumor except for a few cases in which a rapid increase was noticed a few months prior to medical examination. In over 90 per cent of the cases the neoplasm caused no subjective symptoms. There are only a few cases on record in which pain or pressure was felt. There has been only one instance in which there was weakness of the facial nerve [37], and in this case the tumor was found to be intimately wrapped around the nerve.

Clinically, the tumor is indistinguishable from other benign lesions of the parotid gland. Sialography is of no value since the picture of distortion or displacement of the ductal system caused by this tumor is similar to that caused by any other benign neoplasm. Aspiration biopsy is of limited use since it is sometimes difficult to procure representative tissue. There is danger of making an erroneous diagnosis of chronic adenitis, Mikulicz's disease or even lymphoma if the specimen contains only the lymphoid component of the tumor. The most practical method of diagnosis is the microscopic examination of the frozen section at the time of operation.

Grossly, the tumor possesses certain characteristic features which may be of diagnostic value. The tumor is round or oval and often

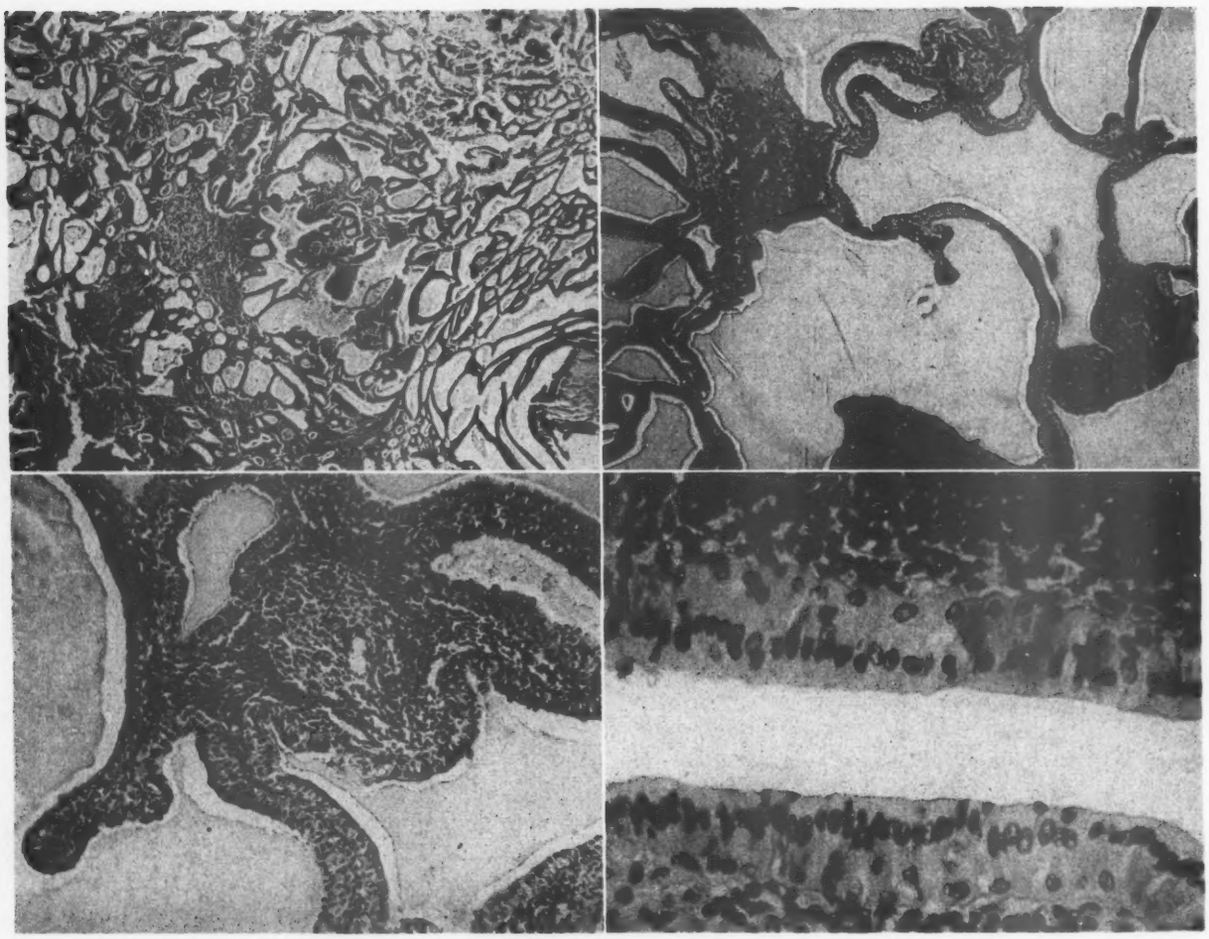

FIG. 3. Photomicrograph showing general morphology of papillary cystadenoma lymphomatosum under low magnification. Note the characteristic intracystic papillary projections and distribution of lymphoid stroma.

FIG. 4. Photomicrograph showing dilated cystic spaces filled with colloid-like fluid. Note papillary projections and lymphoid stroma with prominent germinal centers.

FIG. 5. Photomicrograph showing typical two-layered epithelium lining the cystic spaces, papillary projections and tubules.

FIG. 6. Photomicrograph showing the detailed arrangement of epithelial cells. Note the inner layer of tall columnar cells with deeply stained nuclei arranged toward the luminal end. The cells of the basal layer are cuboidal with large vesicular nuclei.

flattened. It is surrounded by a thick, strong, glistening capsule. Rarely, the tumor may infiltrate the surrounding gland. The surface may be smooth or lobulated and is commonly pink-gray in color. It may be soft and fluctuant or firm or both. The cut surface is studded with whitish nodules corresponding to germinal centers. Also present are irregular cystic spaces filled with fluid and containing papillary projections. The fluid may be clear, serous, milky, mucoid or chocolate colored.

Microscopically, the essential components of the neoplasm are epithelial parenchyma and lymphoid stroma. (Fig. 3.) The parenchymatous tissue is made up of tubules and dilated cystic spaces into the lumina of which project slender, finger-like papillary processes giving the neoplasm its characteristic appearance. (Fig. 4.) In most typical arrangement the epithelium lining these structures is composed of two rows of cells. (Fig. 5.) The inner row is composed of tall columnar cells with oxyphilic granular cytoplasm and the outer layer of cuboidal, polygonal or rounded cells. (Figs. 6 and 7.) The nuclei of the inner layer tend to be deeply stained and are arranged in an even fashion toward the luminal end. The nuclei of the basal cell layer are round or spheroidal and

vesicular with a distinct nuclear membrane and one or two nucleoli. Occasionally the epithelium may be a single layer thick or it may be piled up into several layers without any distinct pattern. Although the tall eosinophilic cell constitutes the predominant cell type, other cells are found here and there lining the spaces. In fact all of the epithelial elements found in papillary cystadenoma lymphomatosum may be observed in the duct lining of the normal parotid gland. Warthin claimed that the columnar cells possessed cilia. With a few [*8,99,119*] exceptions the majority of pathologists [*28,38,89,112*] deny their presence and attribute the cilia-like appearance to artefacts. Within the tubular and cystic spaces may be found secretory material which is usually granular and pink but occasionally homogenous and colloid-like. Jaffé and others [*26,113*] attributed the secretory phenomenon to the presence of intercellular secretory capillaries. Thompson and Bryant failed to demonstrate the presence of such capillaries and concluded from their studies that the epithelial cells are responsible for secreting this material into the lumens of these spaces. These cells on reaching maturity are extruded into the lumens. Mucus-secreting and goblet cells, although infrequent, have been demonstrated [*28,89*]. Meza-Chavez [*74*] and others [*95*] have shown the presence of clusters of sebaceous-like cells in occasional cases of papillary cystadenoma lymphomatosum. The delicate thin basement membrane separates the epithelium from lymphoid stroma which supports the parenchyma and forms the core of papillary projections. When present in abundant quantities the lymphoid stroma contains numerous germinal centers. The precise significance of the lymphoid component of this tumor is not exactly understood. Martin [*72*] claimed that it plays an active part since it seems to be molded into papillary stalks and tufts without being compressed or distorted by epithelial elements. Others prefer to believe that it is essentially passive and represents the lymphoid tissue of regional lymph nodes [*2,42*] or of the salivary gland itself [*75*]. There are still others who consider it as secondary to neoplastic proliferation [*5*] or as an accompanying chronic inflammatory process [*48,112*].

There are several theories concerning the histogenesis of papillary cystadenoma lymphomatosum. The earlier writers [*21,121*] who grouped it with the congenital cyst of the neck

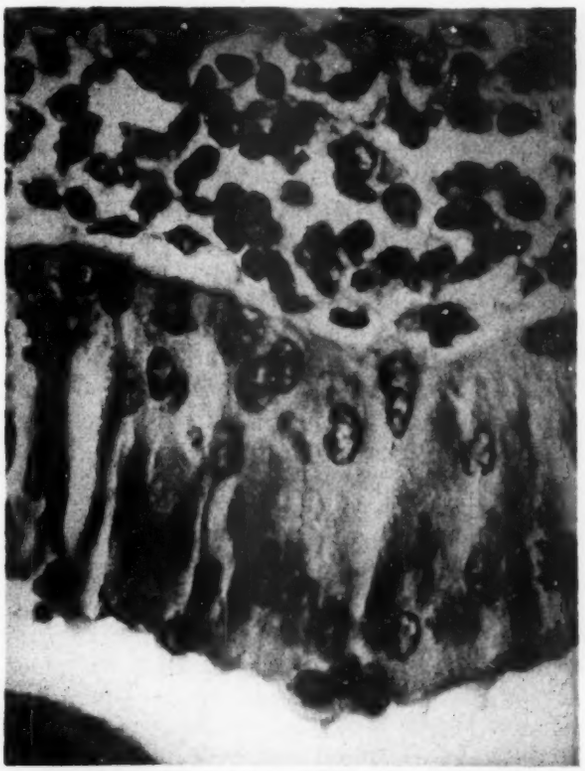

FIG. 7. Photomicrograph of epithelial cells under higher magnification. Note the columnar cells containing oxyphilic granular cytoplasm and thin delicate basement membrane separating epithelium from lymphoid stroma.

attributed its origin to the remnants of thymic anlage and the thymopharyngeal canal. Hildebrand [*50*], supported by several other investigators [*3,98,107*], proposed its origin from the remnants of branchial pouches. Warthin [*118*] suggested that the tumor may arise from heterotopic pharyngeal endoderm, possibly the eustachian tube. However, there is no similarity between the ciliated columnar epithelium of the branchial cysts and fistulas (derived from the remnants of branchial pouches) and eustachian tube on one hand and that of papillary cystadenoma lymphomatosum on the other hand. Meyer [*77*] believed that the epithelial-like lining in this tumor represented hypertrophic endothelium in diseased lymph nodes. This theory is hardly tenable since the epithelial nature of the lining in this tumor has been well established. Other theories that the tumor may originate from ectopic tonsillar tissue [*63*], lymphoid nests in the salivary glands or from a failure of remnants of undifferentiated salivary gland tissue to fuse with the older ductal system [*76*] have not gained popularity since they lack convincing evidence

in their favor. According to Kraissl and Stout [59] the tumor may arise from an embryonic structure, "the orbital inclusion," which gives rise to the orbital salivary glands in certain carnivora and appears as a vestigial rudiment in the human embryo. The presence of the orbital inclusion in man has been denied by several investigators [31,34,72]. Others [87,112] have refuted this theory on the basis that this tumor should occur more frequently in an area medial to the masseter muscle and mandible and more anterior to the parotid gland if this structure were responsible for the genesis of this tumor. Hamperl and others [37,53,64,123] attributed the origin of the neoplasm to the onkocyte. Jaffé [53] suggested that the tumor may arise from onkocytes in heterotopic salivary tissue included in a lymph node adjacent to the parotid gland. This concept, however, does not explain fully all the features of those cases of Warthin's tumor in which the epithelial component is not of the onkocytic type. In addition onkocytes have not been found in salivary glands in patients under twenty years of age, whereas this tumor has been recorded in a two and a half year old child. Onkocytes are found in several other organs of the body but papillary cystadenoma lymphomatosum is found only in the parotid gland or in its immediate vicinity.

The most plausible theory is that initiated by Albrecht and Arzt [2] and supported by several other investigators [17,19,42,64,82,92,112]. They believed that the neoplastic proliferation of heterotopic salivary gland rests entrapped in lymph nodes adjacent to the parotid glands during growth and development may be responsible for the genesis of this neoplasm. The presence of such inclusions has been described previously by Neisse [80], Löwenstein [69a] and Lubarsch [69b], and verified by Thompson and Bryant [112]. Thompson and Bryant have also pointed out the close histologic similarity of the epithelial elements of the neoplasm and the epithelial lining of the ducts of the parotid gland. The chief objection against this theory, that the lymphoid tissue did not represent the histologic characteristics of lymph node, has been satisfactorily resolved by Thompson and Bryant who could demonstrate essential lymph node characteristics of the lymphocytic collections in selected cases of neoplasms.

It is quite evident from a review of the literature that papillary cystadenoma lymphomatosum behaves like a benign neoplasm, has no potentialities to become malignant, and therefore offers an excellent prognosis [31,65,68,107,108]. Six early cases suspected to have undergone malignant transformation either are not authentic cases of papillary cystadenoma lymphomatosum or were found in association with an independent malignant neoplasm. The literature is scant, incomplete and unsatisfactory concerning long term follow-up of 357 cases of papillary cystadenoma lymphomatosum. Of the 105 cases in which a definite follow-up has been listed, at least 12 per cent were followed up for less than a year and 40 per cent for more than a year; in the remaining 48 per cent the duration of follow-up has not been stated. Only seven of these cases seemed to have recurred. Orloff [87a] reported a recurrence rate of 5.5 per cent among 291 cases of papillary cystadenoma lymphomatosum. This is based on the assumption of no recurrence in 191 cases in which there was no follow-up. On the other hand, Foote and Frazell [29] found six local recurrences from surgical procedures on forty-nine tumors among forty-four patients, a recurrence rate of approximately 12 per cent. The recurrence has been attributed either to incomplete removal of the tumor or to its multicentric origin.

A detailed discussion of treatment of this lesion is beyond the scope of this paper. It is sufficient to state that surgical removal of this tumor is the method of choice. The tumor is usually well-defined, is located superficially and is therefore removed without difficulty. In rare instances the facial nerve traverses the growth and poses a problem. A definite diagnosis of the lesion by frozen section examination at the time of operation would eliminate unnecessary radical removal of normal parotid tissue and hazard to the facial nerve. Radiation therapy has been tried in only a few cases and has not proved of any value. It seemed to have reduced the size of the tumor but had not caused its complete regression [56].

SUMMARY

Detailed clinical and histopathologic aspects of 357 cases of papillary cystadenoma lymphomatosum have been reviewed. The neoplasm is found only in the parotid gland or in its immediate environs. It is most commonly located posterior to the angle of the mandible or in front of the lobule of the ear. Like other benign neoplasms it is usually well defined,

grows slowly without causing any symptoms and is freely movable. It is five times more common in males than in females. It chiefly affects individuals between forty-one and seventy years of age, with the highest incidence in the sixth decade. The neoplasm is most commonly found in the white population. Cases have been reported in 4 Japanese, 3 Egyptians, an East Indian and an African Negro but none in the American Negro. The neoplasm is apt to recur when incompletely removed or when present in multicentric foci. Surgery affords an adequate method of treatment. Radiation is of no value. Of several theories concerning the histogenesis, the most satisfactory and well substantiated is that the neoplasm originates from heterotopic salivary tissue enclosed in preparotid lymph nodes.

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The Management of Secondary Cleft Lip Deformities

KERWIN M. MARCKS, M.D., ALLAN E. TREVASKIS, M.D.,* MEREDITH J. PAYNE, M.D. AND JOHN E. KICOS, M.D., *Allentown, Pennsylvania*

IN order to appreciate the full value of methods employed in dealing with the management of secondary cleft lip deformities, we would like to present a series of cases to illustrate what we mean when we stress the fact that "prevention" of these types of deformities is of paramount importance.

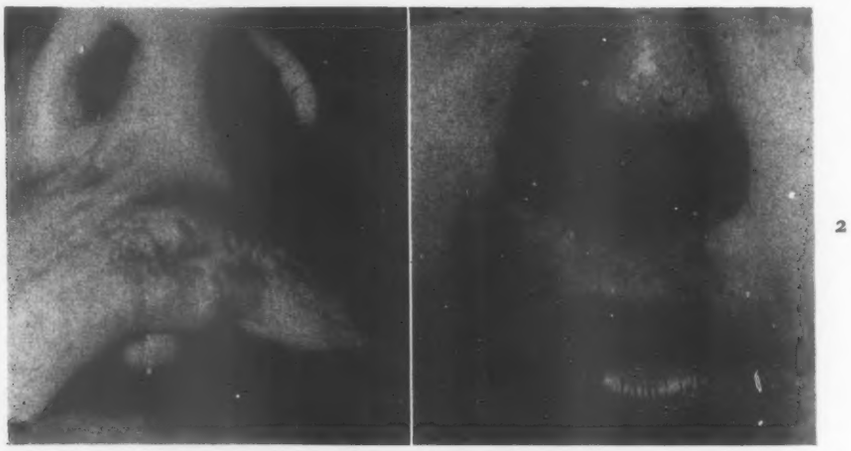

FIG. 1. Case 1. Photograph showing mucous membrane and muscle defect with massive scar deformity at distal end of prolabium. Repair accomplished by muscle adjustment and mucous membrane advancement. Skin-vermilion ridge of prolabium maintained.

FIG. 2. Case 1. Photograph showing completed lip. Note the good condition of the prolabium and why the prolabium should be maintained in the lip at the initial procedure and in all subsequent procedures.

The first group as presented consists of a series of cases with unilateral lip deformities, both complete and incomplete, which were repaired by the method we adopted with modifications in 1951. As one will observe, we are attempting to approach construction of as normal a lip as possible, utilizing the full value of the Cupid's bow and skin-vermilion ridge.

The second group shows the progress made in repair of bilateral lip deformities, utilizing the same principles and again preserving the full prolabium and skin-vermilion ridge which will add considerable length to the horizontal diameter of the lip and prevent a tight lip which is often a distinct characteristic in other methods of repair. We are gathering more and more evidence by clinical research that the prolabium should be part of the lip, and should not be distorted or sacrificed at the initial bilateral lip repair. This is very well illustrated in an old bilateral cleft lip (Case 1, Figs. 1 and 2) in which the prolabium had been maintained initially and secondary repair was simplified. We have also established evidence that skeletal muscle does exist in the prolabium and that there is a growth of hair evident in later life. Because of the importance of this

* Present address: St. Louis, Missouri.

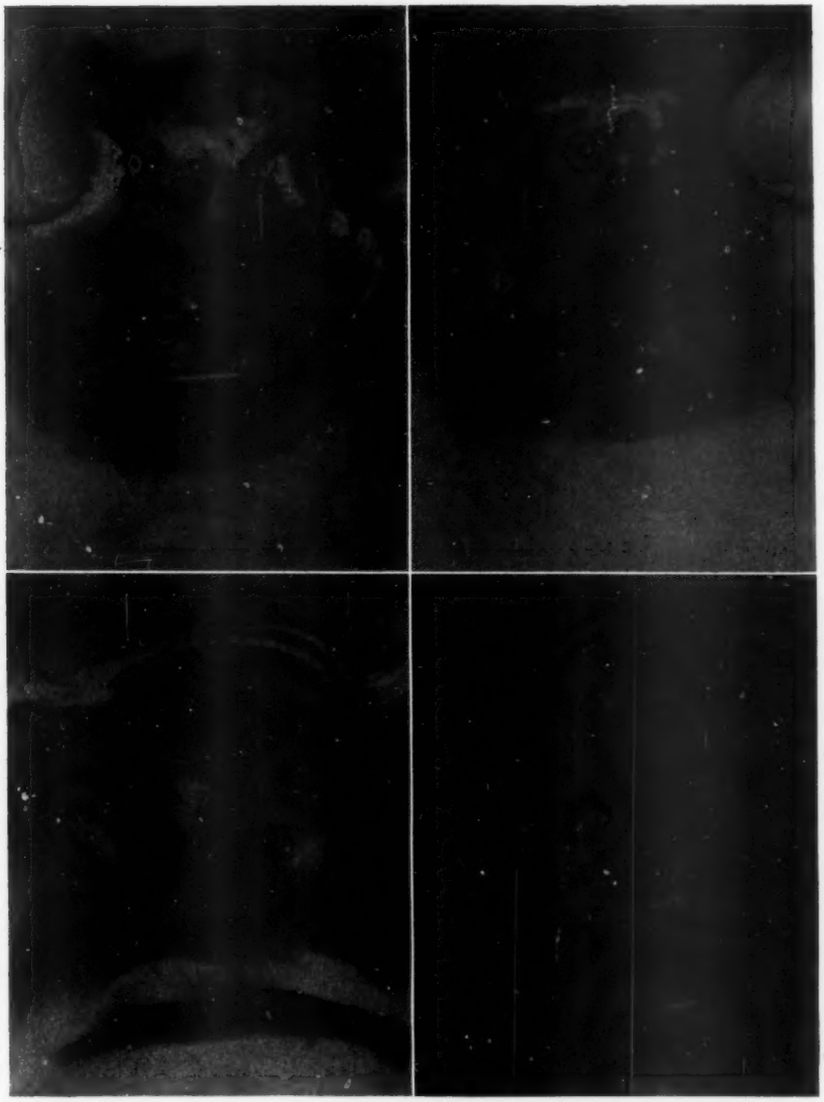

FIG. 3. Case II. Photograph showing labial sulcus adhesions which are frequently encountered. The more severe types do interfere at times with the insertion of orthodontic appliances or replacements and should be repaired.

FIG. 4. Case II. Photograph showing the method employed to correct this defect. The gingival margin is left to granulate. Skin grafts are an unnecessary evil in this location.

FIG. 5. Case III. Shows a mild unilateral lip deformity with short medial and lateral elements but Cupid's bow intact.

FIG. 6. Case III. Shows a repaired lip utilizing a Z-plasty procedure which not only changes the scar line but lengthens both elements.

method in the prevention of secondary cleft lip deformities, we shall elaborate a great deal more in a separate publication. Suffice it to say that we are well pleased with our results to date and we firmly believe this contribution will be a great factor in an attempt to reach a satisfactory solution to this problem.

Either way, we must adopt an attitude of "better attention" to what nature has provided. As soon as we realize this and adhere to the principles of plastic surgery, there will be less scarring and less necessity for performing secondary procedures. True, there will always be some minor adjustments that must be attended to at a later date but nothing compared to what will be presented later. Let us

FIG. 7. Case IV. Shows a slightly more severe deformity which adapts itself very satisfactorily to this Z-plasty procedure.

FIG. 8. Case IV. Shows the completed lip. Note the alignment of the skin-vermilion ridge, the fullness of the lip and an excellent tooth replacement.

FIG. 9. Case V. This case is presented to particularly demonstrate the frequent drooping of the tip of the nose on the affected side. It also demonstrates the malalignment of the skin-vermilion portion of lip.

FIG. 10. Case V. Shows the correction of the nasal tip deformity and formation of a Cupid's bow. We do not use this latter procedure too frequently since it does sacrifice the ridge.

do justice to ourselves and use all our efforts from the very beginning.

TREATMENT

There have been many methods of repair described in the literature. Most are valuable in that they provide a definite foundation for the development and planning of a technic to be used. We are indeed grateful for this help. If we can add just a little bit more to what has already been done, we can truthfully say that we have contributed something to the complete rehabilitation of this type of patient.

The actual treatment of these types of patients depends on the problems that exist. We should like to present the following classification:

Mild Deformities. This type usually involves just the skin or mucous membrane and can be corrected by simple adjustment in the skin-vermilion ridge section, or floor of the nostril. Mucous membrane redundancy is

FIG. 11. Case VI. Note the marked scar deformity existing in prolabium with distortion of skin-vermilion ridge. The occlusion has been satisfactorily restored prior to surgery. The lip appeared to have sufficient tissue present so that we believed an Abbe flap was not indicated.

FIG. 12. Case VI. Shows profile of the patient before operation.

FIG. 13. Case VI. Shows the completed lip repaired by formation of flaps and transpositioning beneath the good portion of the prolabium. Initially the lip was too short in its vertical dimension.

FIG. 14. Case VI. Shows profile of patient after operation.

placed in this category. This is very evident when the patient smiles. A V-Y advancement or a Z-plasty in the horizontal plane is usually sufficient to correct it. Labial sulcus adhesions are frequently encountered. Utilizing mucous membrane coverage for the lip and permitting the gingiva to granulate is our answer to the problem. We have no cases on record in which a skin graft in the labial sulcus was necessary in order to increase the depth of the sulcus. Closure of a small labial fistula can also be included in this group. This can usually be corrected by rebuilding the floor of the nostril anteriorly and advancing the mucous membrane over the repaired defect or by inverting a mucous membrane flap, leaving the base to granulate or provide covering by mucous membrane advancement. (Case II, Figs. 3 and 4.)

Moderately Severe Deformities. These can be classified according to the degree of severity. Case III (Figs. 5 and 6) is an example of the milder variety whereas Case IV (Figs. 7 and 8) is a more severe deformity. The principle in the treatment is the same but the extent of surgery necessary to produce the same effect is more extensive.

Usually this type requires complete reopening of the lip and floor of the nostril. Repair is

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FIG. 15. Case VII. Demonstrates the more severe type of lip deformity where extra tissue is necessary. Note the massive scar deformity in the prolabial region together with the flat lip.

FIG. 16. Case VII. Shows the insertion of the Abbe flap.

FIG. 17. Case VII. Demonstrates the full lip with the scar lines simulating the philtral ridges.

FIG. 18. Case VII. Shows the profile after operation. Note the full pouting upper lip.

accomplished by full advancement of both lip elements to produce as much pouting as possible. Readjustment of the alar base and floor of nostril and Z-plasty to lengthen the medial element, lateral element or both, is performed. With the lip wide open, this is an opportune moment to repair such labial and anterior palatal defects that might exist. Usually there is sufficient nasal mucoperiosteum present to provide lining for the nostril. Since covering is extremely scarce in this region, the raw surface may be left to granulate or a mucous membrane horizontal flap from the upper lip can be transferred over the defect to provide covering.

The initial incision for reopening of the lip always incorporates the scar tissue present on the skin surface of the lip, but we never excise scar incorporated in the mucous membrane of the lip until the final stage of repair. The mucous membrane is frequently deficient and the interdigitation of even scar flaps will help

a great deal. If sufficient, the scar tissue can always be excised at this time.

Frequently there are "touch-up" procedures necessary following the repair for moderately severe deformities. These may incorporate nasal tip repair as well as further skin-vermilion adjustment. One of these methods is illustrated in Case v. (Figs. 9 and 10.) Nasal tip repair is so involved that it must be discussed in a separate presentation.

Severe Deformities. In this category we place the cases in which marked deformity persists and in which readjustment of material still available will be required (evident in Case vi, Figs. 11, 12, 13 and 14), or when extra tissue will be required in order to produce the desired result, either in the form of a full-thickness graft or an Abbe flap. As a rule, we never insert an Abbe flap as an initial procedure. We usually reopen the lip, make all corrections necessary to the underlying structures as described under "Moderately Severe Deformities," repair the lip and wait until all reaction has subsided before insertion of the tissue. This localizes the surface area exposed at the time of the insertion and minimizes the possibility of hemorrhage at some other part of the lip which might interfere with the morbidity of the procedure. We believe that the environment ought to be perfect before insertion of adjacent tissue. The lip elements can be adjusted in proportion at the time of insertion. No V-section of the lower lip should be performed for redundancy until it has definitely been verified that it is not required in the upper lip. This type of flap is well illustrated in Case vii, Figures 15, 16, 17 and 18.

REHABILITATION

The final result will not depend on the surgery itself. We are deeply indebted to the various dental services, speech pathologists and psychologists in the complete rehabilitation of the patient. Surgery is frequently delayed until dental care has been instituted or replacements inserted. Close coordination between these services will determine the efficiency required in the over-all care of this type of patient.

SUMMARY

We have stressed the importance of care and tenderness in the initial repair of a cleft lip deformity as a prevention for secondary lip deformities.

We have presented some procedures that we use in the treatment of lip deformities. Some are original but the most have been contributed, in part at least, by many pioneers in this field. We are indebted to many previous publications. Repair, especially in the unilateral deformity, has incorporated the principles of Z-plasty almost entirely. The angle is variable but the principle is the same.

Coordination between the various services (dental, speech and psychology) has been stressed since it appears to be one of the most important entities in the final rehabilitation of the patient.

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Incomplete Abortions

A TWENTY-FIVE-YEAR REVIEW OF CASES SEEN AT A LARGE MUNICIPAL HOSPITAL

M. Leo Bobrow, M.D., *New York, New York,* and Stanley Friedman, M.D., *Mount Vernon, New York*

Incomplete abortion continues to be the most common diagnosis on an active gynecologic service, especially in a municipal hospital. At Harlem Hospital, New York City, about 800 cases are seen yearly.

Since 1932 all abortion cases have been placed on a separate "abortion service." One visiting physician is given the sole task of treating them. From our early experiences, a clinicopathologic classification of incomplete abortions was devised by Falk [*1*]. (Table 1.) This classification has proved of great value in the diagnosis and management of abortions.

Table 1
1937 classification of incomplete abortions

Type I:	Endometritis—infection is limited to uterine cavity
Type II:	Parametritis—cellulitis of broad ligament; infection has extended to extraperitoneal supporting tissue of uterus
Type III:	Pelvic thrombophlebitis—infection has extended to uterine or ovarian veins
IIIa:	Pelvic thrombophlebitis with embolic manifestations
Type IV:	Abscess of uterine wall—a pathologic rather than clinical entity
Type V:	Septicemia with bacterial endocarditis
Type VI:	Generalized peritonitis—by direct extension from gangrenous tubes and endometrium, or rupture of tubo-ovarian or pelvic abscess
Type VII:	Perforation of uterus

All abortions are considered to be infected. This has been demonstrated frequently by numerous investigators [*2,3*]. It is surprising, however, how little attention is paid to differentiating between an infected and a septic abortion, especially when the treatment and prognosis are so unlike. In brief, the simple infected abortion, type I, is a benign condition with the infection limited to the endometrium. In septic abortions the infection has spread beyond the confines of the uterine cavity, types II to VII.

Extension usually takes place along two routes. One is via the lymphatics and blood vessels of the parametrium and broad ligaments to produce parametritis with or without interstitial salpingitis, and pelvic thrombophlebitis. The second route is by direct extension along the mucous membrane of the uterus into the tubes to produce endosalpingitis. Usually the infection will rapidly spread from here to a pelvic and then a generalized peritonitis. Involvement of an ovary may occur in this process to form a tubo-ovarian abscess.

Even before the antibiotics the simple infected abortion usually resolved spontaneously, whereas the septic abortion had a protracted and complicated course. High fever *per se* is no criterion for sepsis. Many patients with type I abortions enter the hospital with fevers of 104° to 106°F. which drop precipitously with the routine therapy for simple, incomplete abortions. The criteria for differentiating type I from the septic abortions therefore are not the height of the temperature but the presence of extrauterine masses or peritonitis, the findings on blood culture and the clinical course.

In the past year we have been taking a "second look" at abortions in an attempt to determine what effect the antibiotics have had in the pathology, treatment and prognosis of these cases.

Table II gives the incidence of the various types in three sample periods. The years 1932 through 1936 represent the preantibiotic

period, 1946 through 1947 the penicillin period, and 1954 through 1955 the broad-spectrum antibiotic period [*1,4,5*]. The obvious trend is the reduction in the number of septic abortions. Type II and V abortions have become rarities. The incidence of type VII abortion

TABLE II
INCIDENCE OF THE TYPES OF INCOMPLETE ABORTIONS

	1932–1936		1946–1947		1954–1955	
Type	No.	Per cent	No.	Per cent	No.	Per cent
I	901	85.1	1,687	95 2	1,608	98 2
II	98	9.2	29	1.6	2	0.1
III	10	0.9	1	0.05	1	0.06
IV	...	....	.....	.....	.....	.....
V	4	0.4	1	0.05	1	0.06
VI, VI–VII	41	4.0	29	1.6	16	1.0
VII	5	0.5	25	1.5	9	0.6

(perforation) has remained unchanged, as might be expected. Of importance is the fact that the incidence of postabortal peritonitis, type VI and VI–VII, has not been significantly lowered in recent years by the newer antibiotics.

Not accounted for by the original classification has been the progressive rise in the number of cases of postabortal tubo-ovarian abscesses and postabortal endosalpingitis. Formerly these cases went on to generalized peritonitis, but now the antibiotics will sometimes limit the infection to the pelvic viscera with or without pelvic peritonitis. Another new entity that is occasionally seen is the simple endometritis with a positive blood culture. Previously such a case would have led to septicemia and endocarditis, but now antibiotics will rapidly sterilize the blood stream before this takes place. Placental bacteremia, recently described by Studdiford and Douglas [*6*], is thought to be a part of this entity but is more fulminating due to bacterial toxemia.

Thus the antibiotics have virtually eliminated certain postabortal complications and markedly reduced others. In their places some new pathologic types have appeared which are of a less virulent nature. We therefore have revised the original classification, as illustrated in Table III [*7*]. The old type IV abortion, abscess of the uterus, has been dropped because it was never more than a pathologic curiosity and was usually associated with generalized peritonitis.

It should be understood that the infected abortions other than type I may often occur in combination with one another. For example,

TABLE III
REVISED CLASSIFICATION OF INCOMPLETE ABORTIONS—1956

Type I: Endometritis
Type II: Parametritis
IIa: Parametritis with interstitial salpingitis—infection is via lymphatics, sparing endosalpinx; clinically it resembles parametritis but as the parametritis resolves an adnexal mass can be felt
Type III: Pelvic thrombophlebitis
IIIa: Pelvic thrombophlebitis with embolic manifestations
Type IV: Endosalpingitis—infection is by direct extension from endometrial cavity; there may be an outpouring of pus through fimbriated end of tube to produce pelvic peritonitis
IVa: Tubo-ovarian abscess—there may or may not be associated pelvic peritonitis
Type V: Endometritis with bacteremia—diagnosed by positive blood culture; placental bacteremia may or may not be present
Type VI: Generalized peritonitis
Type VII: Perforation of uterus

parametritis (type II) may be associated with type III, IV or VI abortions. In these cases the abortion is usually classified under the most serious type involved since the treatment will be directed primarily toward the graver condition. Thus a case of parametritis with a tubo-ovarian abscess will be classified simply as a type IVa abortion.

In addition, there are certain complications of abortions which are unclassified. These are: (1) acute tubular necrosis (lower nephron nephrosis) due to the ingestion of toxic drugs; (2) clostridial infections without peritonitis; gangrenous metritis may or may not be present but manifestations of toxemia predominate, such as jaundice, renal shutdown, hemoglobinuria and severe anemia; (3) a menigitic syndrome; the spinal fluid may or may not be positive for bacterial growth.

TREATMENT OF ABORTIONS

Type I, Simple Endometritis. Table IV compares results in the treatment of type I abortions in four sample periods [*5,8*].

TABLE IV
RESULTS IN TREATMENT OF TYPE I ABORTIONS

	1936 Pre-curettage and Pre-antibotic Era	1943 Curettage, Pre-antibiotic Era	1946 Curettage and Penicillin Era	1953 Curettage, Broad-Spectrum Antibiotics, Multiple Blood Transfusions
Morbidity*	38%	12%	0.4%	0.4%
Complications	18%	7.2%	0%	0%
Average hospital stay	13.8 days	7.5 days	4.8 days	3.6 days

* 100.4°F. for 2 or more days.

The present treatment of type I abortions consists of antibiotics, oxytocics and prompt curettage. Many physicians are loath to curet a febrile patient, and instead give antibiotics for days in an effort to lower the temperature before performing curettage. It has been shown that it is impossible to sterilize the uterine cavity as long as it contains placental tissue [9]. Therefore if one is certain that the infection is limited to the endometrium, it is futile and in fact dangerous to temporize in emptying the uterus. Procrastination may lead to extension of the infection even while the patient is under antibiotic therapy.

The only time we do not like to curet a patient promptly is when the uterus is over twelve weeks in size or there is a suspicion of a perforation or extrauterine extension of the infection. In the former instance pitocin® infusion and sponge stick curettage will usually reduce the uterus to such a size that it may be curetted without danger. In the latter case the patient must be observed till a diagnosis is certain.

Sometimes when a febrile patient has been curetted, there is a sharp rise in temperature that evening which usually drops to normal by the following morning. Most of our patients are out of bed the evening of the curettage and are ready to leave the hospital the following day. The average hospital stay of these patients is three and a half days [8]. All patients are given supportive therapy as needed.

Type II, Parametritis. The treatment here is antibiotics and oxytocics. We like the combination of penicillin 600,000 units and streptomycin 0.5 gm. twice a day. In cases of penicillin sensitivity one of the broad-spectrum antibiotics is used. Most cases will resolve with antibiotics. After the parametritis has subsided and the patient is afebrile, if bleeding is still present and/or the uterus is still enlarged and boggy, curettage is performed. The danger of lighting up the infection is always present, but if we think there is retained placental tissue, there is no alternative to the curettage. Usually any such flare-ups are short-lived and innocuous.

On rare occasions the parametrial infection may spread retroperitoneally up the lumbar gutter to produce a retroperitoneal phlegmon. Extraperitoneal incision and drainage is the treatment for this complication.

Type IIa, Parametritis with Interstitial Salpingitis. Postabortal interstitial salpingitis is treated the same way as parametritis. Surgery of the adnexal mass is withheld because it will usually resolve without interference with future pregnancies since the endosalpinx has been spared.

Type III and IIIa, Pelvic Thrombophlebitis with or without Emboli. The treatment of pelvic thrombophlebitis consists of antibiotics in large doses. If a positive blood culture is obtained, sensitivity tests should be done to guide one in the choice of antibiotics. We often use a combination of intramuscular penicillin and streptomycin, with intravenous terramycin® 1.0 gm. daily. If the patient shows embolic phenomena, one must consider surgical intervention in the form of ligation of the ovarian veins and inferior vena cava. Delay in such cases may be fatal.

The use of anticoagulant therapy in a patient with embolic manifestations depends largely on the available laboratory facilities. If accurate prothrombin time determinations can be obtained every day, such therapy may stop

TABLE V

MORTALITY FIGURES IN TYPE I, II, III, AND V ABORTIONS

Type	1932–1936			1946			1952–1955		
	Total No.	Deaths	Per cent	Total No.	Deaths	Per cent	Total No.	Deaths	Per cent
I	901	1	0.1	960	2	0.2	3,807	5*	0.1
II	98	4	4.1	13	0	0	5	0	0
III	10	9	90.0	1	0	0	1	1	100.0
V	4	4	100.0	1	0	0	3	2	67.0
Totals.....	1,013	18	1.7	975	2	0.2	3,816	8	0.2

* Three patients died of lower nephron nephrosis (clostridial?); 2 died in shock due to hemorrhage shortly after admission.

further embolization. If the determinations are not accurate, they will either lull one into a false sense of security or produce hemorrhage.

Table V gives the mortality rates for type I, II and III abortions and the old type V, in three sample periods. The persistence of an occasional death from a type I abortion is due to the fact that some patients are not brought to the hospital until they have become moribund from exsanguination. Although proof is lacking in all cases, those patients who died in renal failure probably had clostridial toxemias and hence did not have type I abortions. Deaths from septic complications of type I abortions are no longer seen under our present mode of therapy.

Type IV, Postabortal Endosalpingitis with or without Pelvic Peritonitis. These cases are treated by vigorous medical methods consisting of the following regimen: (1) intravenous fluids and electrolytes with a broad-spectrum antibiotic; (2) penicillin and streptomycin intramuscularly; (3) use of a Miller-Abbott tube with continuous suction; (4) administration of blood for the anemia which is usually present; (5) placing the patient in Fowler's position; (6) charting of fluid intake and output, and frequent blood chemistry determinations; (7) x-ray films of the abdomen for the demonstration of free air under the diaphragm, a foreign body or gas in the uterine wall; physometra, with or without air under the diaphragm, is pathognomonic of a clostridial infection.

If the diagnosis is correct, these patients will usually respond rapidly to treatment with regression of the adnexal masses and pelvic peritonitis if present. Failure of the condition to improve should make one suspicious of generalized peritonitis or retained placental tissue acting as a focus of infection. Generalized peritonitis is indicated by spreading tenderness, rigidity and distention, and a persistently rapid pulse out of proportion to the temperature. Retained placental tissue is manifested by vaginal bleeding and an open cervix through which the tissue can be seen or felt. In the latter case curettage is indicated.

Type IVa, Postabortal Tubo-ovarian Abscess. We are of the opinion that once an ovary becomes infected, whether through gonorrhea, abortion or tuberculosis, the infection can be cured only by surgery. Thus our treatment of the postabortal tubo-ovarian abscess is surgery. The amount of surgery depends on whether or not both adnexa are involved, and the age and parity of the patient. In many cases one adnexa and the uterus can be preserved.

The most important point in treating these cases is the decision when to operate. Formerly we preferred to operate only when the temperature, white blood count and sedimentation rate were normal for some time and remained so after pelvic examination. Since 1945, however, we have been practicing prompt intervention if no improvement is manifested after forty-eight hours of conservative treatment as outlined heretofore. The greatly reduced duration of illness and the less dense adhesions outweigh the disadvantage of operating on a "hot" case, the main disadvantage here being the possible spread of an infection which nature is attempting to localize. Actually it would seem that removal of the focus of infection

would give the body defenses a better chance to control the process.

In the early stage of this disease the patient is acutely ill with peritoneal signs and fever. However, adhesions are still fresh and a plane of cleavage can be obtained with comparative ease. There may be considerable oozing due to friability of the tissues. Later when the abscess begins to resolve there is usually a large amount of induration of the tissues surrounding it, and any attempt to remove it at this stage is fraught with danger, especially to the ureter. Thus if nothing is done in the early acute stage and the patient improves, we must wait till the period when resolution is as complete as possible, i.e., when there is little or no induration. At this time the patient is no longer acutely ill and is a fair surgical risk. However, adhesions are usually quite dense and the pelvis may even be "frozen." This type of surgery may be the most difficult encountered in gynecology, except for advanced pelvic tuberculosis and extensive endometriosis. Another disadvantage of operation at this stage is that the patient has been subjected to a prolonged hospital stay with loss from job or family. In addition, resistance to antibiotics may also develop during their prolonged administration.

Objection may be raised that some of these patients, especially the younger ones, may not require surgery if treated conservatively. We have all seen large inflammatory adnexal masses disappear rapidly with antibiotics and bed rest. Such observations are usually made in cases of pyosalpinx due to gonorrheal infection or in type II and IV abortions. If the infection is postabortal and the ovary is involved, prompt regression of the adnexal mass is not seen.

A word about the ruptured tubo-ovarian abscess: Sometimes a patient with such an abscess being treated conservatively will show apparent improvement, and then abdominal pain and fever will suddenly develop and she will go into collapse. Examination will reveal generalized peritonitis, and the previously palpable tubo-ovarian abscess may or may not be felt. This picture indicates rupture of a tubo-ovarian abscess with the sudden release of pus into the abdominal cavity. These cases must be treated by immediate surgery. The mortality is 100 per cent if there is more than a six- to twelve-hour delay in operating.

Type V, Simple Endometritis with Positive Blood Culture. These cases are treated by antibiotics as determined by sensitivity tests on the organism obtained from the blood culture, and curettage. We have not seen any cases with persistently positive cultures.

Type VI and VI–VII, Generalized Peritonitis with and without Perforation. Table VI gives the results of our treatment over a twenty-five-year period [*1,4,10*]. In the beginning the few supportive measures then available were of no value. The first instance of recovery from proved postabortal peritonitis occurred in 1940 when a laparotomy was performed on a patient misdiagnosed as having a ruptured ectopic pregnancy. A supracervical hysterectomy and bilateral salpingo-oophorectomy with splitting of the cervix and drainage into the vagina were performed. The patient recovered and left the hospital in twelve days with only a superficial wound infection. In the following years a method of treatment was tried as a compromise between medical and surgical treatment—incision and drainage. This was performed three times without success, and so in 1943 it was decided to treat half the cases surgically and half medically or conservatively.

As Table VI shows, 55 to 60 per cent of the patients recovered when operated upon, whereas none recovered if not operated upon. In 1946 we began treating all cases of postabortal peritonitis by immediate surgery. Since results with total hysterectomy were not as good as with supracervical hysterectomy, total hysterectomy was not performed routinely. Our salvage rate continued to be about the same until the broad-spectrum antibiotics became available. In conjunction with immediate surgery, our recovery rate rose to 92 per cent.

At this time we began to wonder if these new drugs might not be able to effect a cure without resorting to surgery, and a new approach to the management of these cases was instituted. Instead of immediate surgery, all patients with generalized postabortal peritonitis were given large doses of antibiotics for as long a time as they seemed to be holding their own. In many cases there would be some initial improvement, as manifested by a drop in temperature and reduced distention, tenderness and rigidity. However, the pulse remained rapid, with some fullness of the abdomen. The patient's condition would then vary from day to day for a few days and then the patient would invariably go into toxic collapse. Surgery

TABLE VI

RESULTS IN TREATMENT OF TYPE VI AND VI–VII ABORTIONS

	Total Cases	No Operation	Recovered	Operation	Type of Operation	Recovered	Recovery Rate (Per cent)
1932–1936 (pre-antibiotic, nonoperative era)	41	41	0	0	.....	...	..
1941–1942 (sulfa drugs)	12	9	0	3	Abdominal incision and drainage	0	0
1943–1945 (transition to immediate surgery)	20	13	0	7	Supracervical hysterectomy, 5	4	57
					Total hysterectomy, 2	0	
1946–1947 (immediate surgery and penicillin)	17	1	0	16	Supracervical hysterectomy, 15	7	56
					Total hysterectomy, 1	1	
1952–1953 (immediate surgery and broad-spectrum antibiotics)	15	2	0	13	Supracervical hysterectomy	12	92
1954–1955 (era of procrastination)	16	3	0	13	Supracervical hysterectomy, 11	8*	62
					Total hysterectomy, 2	0	
1956 (return to immediate surgery)	5	0	0	5	Supracervical hysterectomy	4	80

* Of the operative deaths, 4 patients had been treated conservatively from 2 to 9 days before operation.

in these cases was often of no avail because of the duration of the peritonitis. As a result of this approach our recovery rate dropped back to 62 per cent, which was almost the same as the rate before the use of antibiotics.

In other words, although the antibiotics might mask or temporarily suppress postabortal peritonitis, they obviously could not effect a cure. We therefore abandoned this method of treatment and returned to the practice of immediate surgery, with certain limitations.

At the present time, once we consider the diagnosis of a type VI or VI–VII abortion, we institute the routine outlined in the treatment of type IV abortions. Oxygen is often needed in addition to the other measures. After twelve hours of this therapy the patient is re-evaluated. If there has been considerable improvement, we continue this treatment. If the patient's condition has not improved or if the improvement is equivocal, surgery is performed. If at any time under the conservative treatment continued steady improvement is not seen, this treatment is abandoned. The physician in attendance must have the courage to act decisively. These patients are usually toxic and appear as poor risks. There is a great tendency on the part of the attending physician to temporize and place undue reliance and hope on the antibiotics. However, if there is not an obvious progressive improvement under the therapy outlined heretofore, further delay in operating is associated with a rapidly rising mortality rate. The recovery rate under this program rose to 80 per cent in 1956.

Sometimes a patient will be admitted in a state of septic shock. In these cases the usual twelve-hour period of conservative treatment is not given but the patient is operated upon as quickly as possible. From the time the patient is admitted to the time the surgery can be performed we are usually able to administer some blood, fluids and antibiotics, as well as being able to relieve some of the distention. A vasconstrictor such as levophed® is also used to raise the blood pressure. The mortality rate in this type of patient is 100 per cent without surgery. Surgery will salvage some.

This is one phase of gynecologic surgery in which speed is essential because of the poor condition of the patient. Therefore the cervix is not removed unless a clostridial infection is present. In this instance a focus for continued

toxemia may lie in the cervix and it should be removed. Sometimes in very young patients we try to save an adnexa if it appears only minimally involved. This entails a certain risk and requires considerable judgment. For example, even though a tube and ovary may still look good, the infundibulopelvic ligament must be carefully inspected. If it is edematous and indurated, there is a good chance that its vessels may already harbor thrombi. Leaving the adnexa and vessels behind may then leave the patient vulnerable to pelvic thrombophlebitis, embolism and retroperitoneal phlegmon. When in doubt it is best to remove the adnexa, no matter what the age of the patient. We all would prefer a live patient without ovaries to a corpse with one.

Technic often cannot be followed in this type of surgery. All the tissues are edematous and friable; sutures will cut through and clamps cannot be used. Despite all this the surgery can and should be completed in an hour. Collections of pus between loops of bowels should be evacuated, the lumbar gutters explored and the liver palpated for subphrenic and subhepatic abscesses. Drainage is accomplished by splitting the cervix or opening the cul-de-sac and bringing Penrose drains into the vagina. A Mikulicz packing is sometimes used to control oozing from the operative site. The abdomen is closed in layers and a drain is placed subcutaneously as a prophylaxis against wound infection.

The postoperative course is directed toward deflation of the gastrointestinal tract, and maintenance of nutrition and fluid and electrolyte balance. The skin drain is removed in forty-eight hours and shortening of the vaginal drains is begun in ninety-six hours.

When one has seen a moribund patient make an uneventful recovery and walk out of the hospital ten days after one of these procedures, further proof of the value of surgery seems superfluous.

Type VII, Perforation of the Uterus. A perforation *per se*, without signs of hemorrhage, intra-abdominal injury or infection, is treated with antibiotics and close observation. The patient is given nothing by mouth and oxytocics are usually withheld because of the danger of forcing some infected uterine contents into the abdominal cavity. These cases usually respond well to this sort of therapy. Curettage is avoided unless there is profuse hemorrhage due to retained placental tissue which is easily reached. In such a case a sponge stick is gently used to remove this tissue.

If there is x-ray evidence of a foreign body in the abdomen, laparotomy is performed at once. Sometimes catheters and other objects may be in the abdomen for several weeks with minimal peritoneal reaction. Administration of antibiotics before hospitalization may have helped in limiting the spread of infection here. Often the omentum is wrapped around the foreign body, walling it off completely from the rest of the abdomen. At laparotomy if there is no evidence of peritonitis or visceral injury, nothing more than removal of the foreign body need be done. The hole in the uterus can be débrided and closed if present; often it cannot be found.

The question of curetting these patients is often raised. If the uterus is still enlarged and contains a large amount of placental tissue, curettage is performed after closing the abdomen.

The prognosis in type VII abortions without peritonitis and visceral injury is excellent.

Unclassified Types. (1) Acute tubular necrosis due to a toxic drug is treated medically. (2) Clostridial infection without gangrenous metritis or peritonitis but with manifestations of toxemia is treated by curettage, antibiotics and polyvalent antitoxin; concomitant renal shutdown is treated medically. If there is a gangrenous metritis, total hysterectomy and bilateral salpingo-oophorectomy are performed. (3) The meningitic syndrome is treated medically.

CONCLUSIONS

A review of the Abortion Service of the Harlem Hospital, New York City, is presented. This review represents the experiences of twenty-five years and includes approximately 15,000 cases of abortions of less than sixteen weeks' gestation.

Because of the large numbers of these cases with their many complications they are divided into various categories or "types" on a clinicopathologic basis. These categories are used as a reference in the diagnosis and management of the abortions.

Antibiotic and chemotherapeutic agents have altered the pathology of abortions, necessitating changes in the original classification. It is anticipated that newer antibiotics and other

drugs will produce further changes in the pathogenesis and pathology of postabortal infections.

The treatment of the different types of abortions is given, with our results. Antibiotics have reduced the mortality and morbidity in the less severe types of infections to a minimum. They have also succeeded sometimes in limiting the more severe infections to the pelvis. Once generalized peritonitis has developed, however, prompt surgery offers the best hope for recovery. Reliance on the antibiotics in these cases is usually catastrophic.

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Carcinoma of the Duodenum

REVIEW OF THE LITERATURE FROM 1948 TO 1956

H. L. P. RESNIK, M.D. *New York, New York,* AND DONALD R. COOPER, M.D., *Philadelphia, Pennsylvania*

PRIMARY carcinoma of the duodenum has been an almost uniformly fatal disease. Reports of five year survivals following definitive surgical treatment include only seven patients [*2,4,43*], and careful classification of the origin of the tumor might well disqualify five of them [*2,4*]. Upon reviewing the literature, the reasons for these poor results seem to be twofold. First, the inability of both the clinician and the roentgenologist to suspect and establish the diagnosis when the lesion is surgically accessible has been disappointing. The surgeon in turn has added to this dismal survival rate by an unusual reticence to attack this lesion as aggressively as he does other gastrointestinal carcinomas. Considering the recent advances in both roentgenologic diagnosis and surgical extirpation of malignant tumors, the lack of progress in this particular lesion would appear to be all the more unusual. For these reasons it is the purpose of this paper to briefly review the diagnosis and treatment of this lesion, to bring up to date the literature on this subject, and more particularly to review the experience of a large city hospital with carcinoma of the duodenum.

INCIDENCE

Review of the literature through 1948 (Table I) has been thorough and well accepted. There have been 453 documented cases of duodenal carcinoma. Since then, however, as medical literature has become more voluminous, there have been conflicting reviews. Schwarz [*40*] adds thirty cases through 1951 alone. Yet in reviews from 1948 to 1954 Freedman [*17*] reports only fifteen new cases, Seeley and Campbell [*41*] report seventy-three cases and add two of their own, and Brenner and Brown [*3*] accepted twenty-five cases and added fifteen more. These different estimates in papers reviewing the same literature are confusing.

Because of this discrepancy it was decided to review the English literature for the past seven years to see if a more accurate estimate could be compounded. During this period, it was found that 163 cases were added to the literature, of which 118 are acceptable under the criteria originally described by Stewart and Lieber [*48*]. From 1907 through 1957, twenty-three patients with duodenal carcinoma have been seen at the Philadelphia General Hospital, fourteen of whom have been previously reported [*25,26,48*]. We shall report at this time the nine cases seen at this institution since 1938. This would make a total of 580 cases reviewed to date, if the 453 previously reported cases are entirely acceptable. (Table I.)

PATHOLOGY

Mateer and Hartman [*29*] have divided lesions of the duodenum into suprapapillary (from pylorus to ampulla of Vater), peripapillary (the mucosa of the duodenum about the ampulla) and infrapapillary (below the ampulla to the duodenojejunal flexure). We agree with Dixon et al. [*9*], Brenner and Brown [*3*], and Burgerman et al. [*6*] who believe that ampullary lesions should not be included with duodenal carcinomas since malignancies may arise from the common bile duct or the ducts of Wirsung and Santorini. Peripapillary lesions can usually be classified as predominantly above or below the ampulla. This view would be supported by Lieber, Stewart and Lund [*25*] who analyzed 229 peripapillary and/or ampullary lesions and were able to accept only three cases as clearly derived from intestinal mucosa. (Table II.)

It must be admitted that primary carcinoma of the duodenal mucosa may on occasion

TABLE I
REVIEW OF ACCEPTED CASES OF DUODENAL CARCINOMA

Reference	No.	Suprapapillary	Peripapillary	Infrapapillary
Stewart and Lieber, 1937	323	63	222	38
Berger and Koppelman, 1942	63	14	29	20
Kleinerman, Yardumain and Tamaki, 1948	67	25	17	25
Total	453	102	268	83
From 1948 to 1956	118	46	11	61
Present study	9	4	.....	5
Total	580	152	279	149
Lieber, Stewart and Lund, 1939	−219	...	−219	...
	361	152	60	149

involve the ampullary area by direct infiltration. With the biliary tree, pancreatic duct and the ampulla of Vater all involved in such a tumor it is difficult, if not impossible, to determine in which organ the tumor originated. The great preponderance of peripapillary tumors reported would suggest that many are actually tumors arising from the ampullary or ductal structures. In order to eliminate such confusion we shall speak only of supra and infrapapillary lesions of the duodenum.

Applying this premise to Table I and subtracting the cases re-assessed by Lieber, Stewart and Lund [*25*] the number of reported peripapillary lesions falls to sixty, and the incidence of proved malignancy of the duodenum is cut almost 40 per cent. It would appear further that duodenal lesions are distributed equally above and below the ampulla of Vater.

SIGNS AND SYMPTOMS

The lesion may be seen as early as the third decade but most commonly in the fifth and sixth. There does not appear to be any predisposition to race or sex. Although some believe this tumor is three times as common in males, in our series the proportion is three males to six females.

With the prevalence of upper gastrointestinal symptomatology and the present day proneness to obtain x-ray study, carcinoma of the duodenum may be seen before the late complications of this lesion augment its diagnosis. The usual symptoms associated with malignant disease, i.e., weakness, weight loss, anorexia and anemia are present.

There are no characteristic signs or symptoms consistently demonstrated with this lesion although some authors report a relationship between the presenting complaints and the location of the lesion. Ochsner and Kleckner [*34*] have reported that suprapapillary tumors produce symptoms of pyloric obstruction, and infrapapillary tumors symptoms of gastrointestinal hemorrhage. Brenner and Brown [*3*] on the contrary found that infra-

TABLE II
ANALYSIS OF 222 PERIPAPILLARY TUMORS
(AFTER LIEBER, STEWART AND LUND)

Group	Diagnosis
I	Primary carcinoma of the ampulla of Vater (1 case)
II	Primary carcinoma of the terminal duct of Wirsung (3 cases)
III	Primary carcinoma of the terminal bile duct (7 cases)
IV	Primary carcinoma of the intestinal mucous membrane covering the papilla of Vater (3 cases)
V	Carcinoma involving all the epithelial structures of the papilla of Vater under groups I, II, III and IV (182 cases)
VI	Carcinoma involving all the epithelial structures comprising the papilla of Vater as before, exclusive of the intestinal mucous membrane (33 cases) groups I, II and III.

papillary lesions caused obstruction more frequently than did suprapapillary tumors and noted no correlation between the site of lesion and hemorrhage. Table III indicates that ulcer-like pain, nausea and vomiting are seen equally with both types of lesions, but that signs of gastrointestinal hemorrhage are seen in almost half the infrapapillary cases.

TABLE III
CARCINOMA OF DUODENUM
(LOCATION OF LESION VERSUS PREDOMINANT SYMPTOM COMPLEX)

Symptoms	Supra-papillary	Infra-papillary
Ulcer-like pain	10	8
Nausea and vomiting	11	12
Jaundice	2	7
Gastrointestinal hemorrhage (anemia) (melena)	7	19
Total	30	46
Total reviewable histories (from 1948 to 1956)	35	52

In our nine patients, four had suprapapillary and five infrapapillary carcinomas. Table IV reveals that vomiting was a presenting symptom in eight of the nine patients but that melena and anemia were most commonly seen in the patients with infrapapillary lesions. We believe that it is more important to recognize the four prime symptom complexes by which this lesion may present than it is to identify them with an anatomic location. These complexes may be grouped as follows:

Ulcer-like syndrome. The pain pattern may suggest peptic ulcer disease, but duodenal malignancy rarely awakens the patient at night. It is more commonly characterized by boring into the back and is rarely complicated by hematemesis. It does not respond to an ulcer regimen (six of nine patients) (Table IV.)

Gastrointestinal hemorrhage. This is manifested by weakness and tarry stools associated with anemia. Seven of nine patients reported this (100 per cent of the infrapapillary lesions). Hematemesis was present in two patients.

Obstruction. This is suggested by early satiety, anorexia and vomiting, and was seen in eight of the nine patients.

Jaundice. This is evident in lesions which are primarily ampullary or have extended to involve the ampulla. No patients in this report were so affected.

The presenting symptom complex is a func-

TABLE IV
SUMMARY OF PATIENTS SEEN AT THE PHILADELPHIA GENERAL HOSPITAL FROM 1948 TO 1956

Case	Age (yr.)	Race	Sex	Location of Lesion	Presenting Symptom	Procedure	Follow-up
I	67	W	F	Suprapapillary (second)	Anemia, periumbilical pain, weight loss	Palliation	Died, 18 days
II	84	W	M	Suprapapillary (second)	Vomiting, epigastric pain, weight loss, mass in right upper quadrant	Palliation	Died, 6 mo.
III	64	W	M	Suprapapillary (second)	Persistent vomiting, weight loss	Palliation	Died, 14 days
IV	56	N	F	Suprapapillary (second)	Vomiting, weight loss, anemia	None	Died, 3 days
V	58	N	F	Infrapapillary (third)	Epigastric pain, vomiting, melena, anemia	None	Died, 2 days
VI	72	W	F	Infrapapillary (third)	Vomiting (hematemesis), melena, epigastric pain	Palliation	Died, 5 mo.
VII	35	N	F	Infrapapillary (fourth)	Vomiting, weight loss, melena	Palliation	Died
VIII	83	W	M	Infrapapillary (third)	Vomiting (hematemesis), melena, sub-xiphoid pain	None	Died, 18 hours
IX	51	N	F	Infrapapillary (third)	Weight loss, melena, vomiting, severe anemia, pain in the left upper quadrant	Pancreatico-duodenectomy	Died, 9 mo.

tion more of the growth tendency of the malignancy than its location, the annular and polypoid growths obstructing and the ulcerating lesions causing bleeding. We agree with Dixon [9] who states "Reviewers have devoted much effort to the differentiation by symptoms of lesions of the suprapapillary, peripapillary and infrapapillary regions of the duodenum. They have gone into great detail . . . We might say that one is doing well if one suspects the presence of a lesion . . . strongly enough to suggest roentgenologic examination."

X-ray appears to be the only definitive method of diagnosis. In the fourteen patients at Philadelphia General Hospital prior to 1938 only one underwent an upper gastrointestinal x-ray and demonstrated duodenal obstruction. Since 1938, however, eight of our nine patients had appropriate x-ray studies and in all save one, the diagnosis was suggested preoperatively. In the past twenty years the Radiology Department at the Philadelphia General Hospital has performed approximately 45,000 upper gastrointestinal examinations [33]. This lesion was noted once in every 5,000 studies, an incidence six times more common than stated by Feldman [14]. It would appear, that although the autopsy incidence is only 0.033 per cent of 350,186 postmortem examinations [13,22], clinical selection will bring this lesion to the attention of the radiologist more frequently than this figure would imply.

TREATMENT

The treatment of this lesion is surgical excision. In former years diagnoses were made so late that when patients came to surgery palliation in the form of by-pass was all that could be offered. At the Philadelphia General Hospital five of the six patients who came to surgery received palliation. Since the growth of this malignancy is one primarily of extension via lymphatic drainage from the superior and inferior pancreaticoduodenal and gastroduodenal lymph nodes to the hepatic nodes, and somewhat less to the superior mesenteric chain, a block resection including these structures should be the treatment of choice.

In 1942 Berger and Koppelman [2] reviewed 386 cases in seventy-six of which radical surgery has been performed. The five-year cure rate was only 5.2 per cent which represented peripapillary lesions only. Whether or not these cases were involved in the revision offered by Lieber, Stewart and Lund [25] cannot be ascertained, but statistically it would be very likely that these lesions were not clearly duodenal in origin.

In comparing the figures of Berger and Koppelman [2] and our review of the past seven years, it can be seen that the percentage of cases coming to surgery is similar (about 50 per cent) but that there appears to be an increase in the number of patients in whom radical surgery is undertaken (38 per cent in the series to 1942, and 52 per cent in the past seven years) (Table v.) Because of the rarity of pancreaticoduodenectomy before 1940, we must infer that the radical surgery implied by Berger and Koppelman [2] was primarily segmental resection.

TABLE V
A COMPARISON OF OPERABILITY OVER THE PAST 50 YEARS

	Berger and Koppelman (to 1942)	From 1948 to 1956
Total number of patients.....	386	127
Patients operated upon.....	196 (50%)	63 (49%)
Palliative operation only.....	106 (54%)	16 (27%)
Attempted radical resection...	76 (38%)	33* (52%)

* Not including segmental resection.

Brunschwig and Tiholiz [5] reviewed the literature to 1945 and found twenty-three cases reported, with one five-year survival following resection. They described three approaches to duodenal carcinomas, local resection of tumor, segmental resection of the duodenum with or without a portion of the adjoining pancreas, and pancreaticoduodenectomy. Reporting on five cases in which three segmental resections and two pancreaticoduodenectomies were performed, they had one five-year survival. Ebert et al. [12] reported two cases in which segmental resection of what appeared to be well localized tumors resulted in recurrences after two- and three-year intervals and he believes that pancreaticoduodenectomy was indicated initially.

Shallow, Wagner and Manges [44] added to the review of infrapapillary lesions and found only 23 per cent of the patients alive after one year and 7 per cent alive after three years. Brenner and Brown [3] did not find a significant difference in survival between palliative and attempted curative procedures.

Advances in anesthesia, and pre- and post-operative care plus more awareness on the part of the patient allow us to undertake extensive surgery sooner and with much less operative mortality. Cancer surgery implies removal of the lesion and its usual foci of spread. Although the survival rate following pancreaticoduodenectomy has been attended by discouraging follow-up figures at present, it would seem that the only hope for improvement in the treatment of this lesion lies in earlier diagnosis and more extensive surgical removal. With pancreaticoduodenectomy more commonly employed in the future than in the 60 per cent of the operable patients reviewed since 1948 we might better the five-year survival rate.

In our series six of nine patients were operated upon. Palliation alone was attempted in 83 per cent. None of these patients lived longer than six months. (Table 1.) The one patient in whom a curative type procedure was attempted is presented herein in detail.

CASE HISTORY

The medical history was obtained from the patient's sister as the patient was unable to speak intelligibly. She had been in good health until one year prior to admission when she had a "stroke" and was unable to use her right arm and leg, and to speak or swallow. Since then she has partially recovered each of these functions. In the past two months progressive shortness of breath and ankle swelling had developed. Her stools had been tarry for the previous two months, and she tired easily. She was admitted to the hospital on November 27, 1956, with persistent left upper quadrant pain, unrelieved by food or drink. Examination revealed a fifty-one year old Negro woman who appeared older than her stated age and exhibited evidence of recent weight loss. Her mucous membranes were nearly white. There was a grade 2 systolic precordial murmur. Her abdomen was full, had normal bowel sounds and no tenderness. A questionable epigastric fullness was palpated. There was 2-plus pitting edema of her ankles. The neurological examination exhibited a left facial weakness and weakness of the right arm and leg. There was a positive Babinski reflex on the right. The patient had dysphonia and swallowed with effort.

Laboratory data revealed a hemoglobin of 2.1 gm. per cent; hematocrit, 10 per cent; white blood cells, 10,000 per cu. mm.; stool for occult blood was 4 plus.

The patient received four transfusions of 500 cu. cm. of whole blood which brought her hemoglobin level up to 7.7 gm. per cent. Proctoscopy and barium enema examinations were negative. The upper gastrointestinal examination was interpreted as a filling defect of the infrapapillary duodenum probably due to malignant tumor. The patient was transfused to 11.2 gm. per cent of hemoglobin and her edema and cerebration cleared markedly. She was operated upon December 17, 1956, and a firm fixed mass involving the third and fourth portions of the duodenum was found. The liver was free and no obvious nodal metastases were noted although there appeared to be extension into the head of the pancreas. A sub-total pancreaticoduodenectomy was effected.

The patient had an uneventful postoperative course and was asymptomatic for six months. In June of 1957, obstructive jaundice developed and she died of recurrent carcinoma in August, 1957, eight months following original resection.

The pathologic specimen demonstrated an annular adenocarcinoma originating in the third portion of the duodenum. No positive nodes were found.

CONCLUSIONS

1. The literature from 1948 to 1956 has been reviewed and 118 cases of carcinoma of the duodenum have been found acceptable, to which have been added nine cases. The total number of cases is now 580.

2. Peripapillary carcinoma is misleading and as such should not be considered a classification of carcinoma of the duodenum. This would make 219 cases previously reported as duodenal carcinoma unacceptable. The total of accepted cases after revision is 361.

3. Obstructive symptoms may be associated with any lesion of the duodenum but gastrointestinal hemorrhage is most often seen with infrapapillary lesions.

4. Since palliative operations and segmental resections have not been effective, it is proposed that all resectable carcinomas of the duodenum be treated by pancreaticoduodenectomy in an effort to improve the survival of the patients.

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Brachial Plexus Block

F. Paul Ansbro, M.D., *Brooklyn, New York,* Albert E. Blundell, M.D., *Kew Gardens, New York,* Wilbert E. Hernandez, M.D., *Wilkes-Barre, Pennsylvania,* and James V. Carter, M.D., *Cheyenne, Wyoming*

From St. Catherine's and Adelphi Hospitals, Brooklyn, New York.

For a long time blocking of the brachial plexus has held the interest of the surgeon and, more recently, the anesthesiologist. The value of the procedure has always been evident because a patient who needed operation for a pathologic condition in the upper extremity of necessity had to undergo general anesthesia of some type (inhalation, intravenous); frequently this type was not suitable but nevertheless had to be employed because there was usually no alternative. Many times operative procedures were of such length that the physical economy of the patient was taxed; in other instances the operation was followed by the application of a large-body plaster cast which limited thoracic and diaphragmatic expansion. This in turn was conducive to pulmonary atelectasis because of the prolonged recovery time necessary for long-continued general anesthesia and also on account of constriction of the thorax by the cast. The importance of the patient's assuming an upright position immediately postoperatively was realized. Long continued postoperative narcosis and vital center depression was a deterrent to the uncomplicated recovery from general anesthesia for operations on the upper extremity. In addition, voluntary movement by the patient of the muscles of the extremity during repair of severed tendons and nerves was highly desirable as an aid in correctly approximating the severed ends. The obvious impossibility of the unconscious patient performing these maneuvers rendered the retention of consciousness by the patient of great assistance to the surgeon in doing his exacting work.

Because of these features a method of blocking the brachial plexus was needed which would insure successful block in a dependable number of cases and which would not "wear off" before the operation was finished; this need induced one of us (F. P. A.) to devise a method of continuous brachial block [*1*].

However, since the introduction of new anesthetic agents which produce prolonged effect we have not found it necessary to use the continuous method. Bonica, Moore and Orlov [*2,3*] reported a series of approximately 1,500 cases of surgery of the upper extremity in which brachial block was employed. They obtained prolonged anesthesia with 0.15 per cent pontocaine® (up to six hours). We were unable to duplicate this prolonged effect with pontocaine in any of our cases (usual length two to three hours). However, with nesacaine (1 or 2 per cent) and with a new reblocking technic we were able to obtain anesthesia of any duration we wished.

REVIEW OF LITERATURE

In 1885 Halstead [*4*] performed the first regional anesthesia procedure and indeed performed the first operation under brachial block when he (according to Matas [*5*]) "freed the cords and nerves of the brachial plexus after blocking the roots in the neck with cocaine solution." In 1897 Crile [*6*] carried out a successful block of the plexus which was a combination of surgery and anesthesia. In the supraclavicular area he injected the skin with a weak cocaine solution (0.1 per cent) and by dissection exposed the plexus as it passed over the first rib. Each nerve of the plexus was then directly injected with 1 cc. of cocaine (0.5 per cent) solution. This was referred to as the "endoneural conduction technic" and, as may be imagined, was not used frequently. In 1911 Hirschel [*7*] performed brachial block by the axillary route whereby a needle was inserted through the axilla and carried to the plexus,

carefully avoiding the large blood vessels in the region. (Fig. 1.) This method was modified by Pitkin [8], who employed two needles, one of which he carried beyond the clavicle to the transverse process of the sixth cervical vertebra and a second needle contacted the transverse

FIG. 1. Brachial plexus block by the axillary route. The axillary artery is retracted upward and the needle is advanced behind the artery. (From: LABAT, G., Regional Anesthesia, Its Technique and Clinical Application. Philadelphia, 1928. W. B. Saunders Co.)

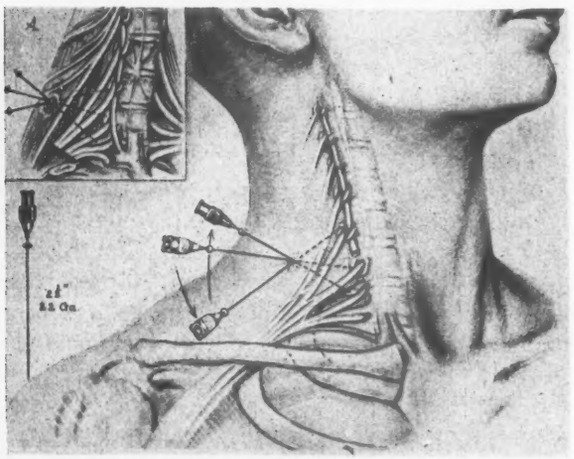

FIG. 3. Brachial plexus block by the lateral route depicting the approach to the posterior tubercle of the transverse process of C6 and C7. A, demonstrates the course of the needle through the substance of the scalenus anticus muscle. (From: Conduction Anesthesia by George P. Pitkin. Edited by Southworth, J. L. and Hingson, R. A. Philadelphia, 1953. J. B. Lippincott Co.

process of the seventh cervical vertebra. (Fig. 2.) The infraclavicular route also was employed. With the patient's arm in abduction

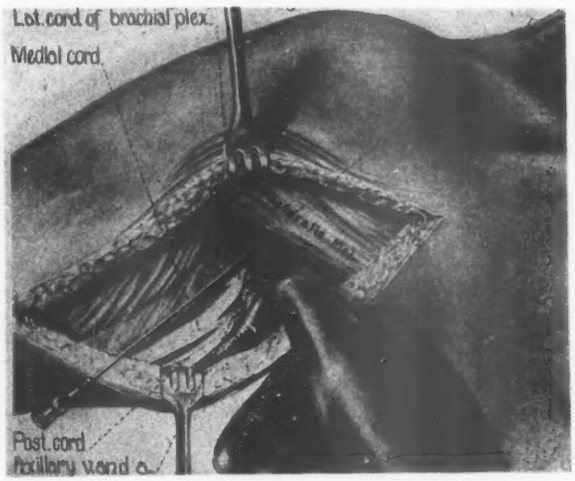

FIG. 2. Brachial plexus block by the axillary route. Axillary dissection depicting the manner in which the axillary vessels are retracted out of the path of the advancing needle. (From: Conduction Anesthesia by George P. Pitkin. Edited by Southworth, J. L. and Hingson, R. A. Philadelphia, 1953. J. B. Lippincott Co.)

the needle was inserted in the vicinity of the coracoid process of the scapula and carried beneath the clavicle in the direction of the tubercle of Chassaignac (transverse process of C6). In 1912 Kulenkampff [9] introduced his supraclavicular method which was destined to become the best approach to the plexus. Pitkin [8] also carried out a lateral approach which resembled the usual cervical plexus block. (Fig. 3.) Kappis [10] developed the posterior, paravertebral approach which is similar to the technic of paravertebtal block in the lower regions of the spine. (Fig. 4.) The needle is inserted 2 to 3 cm. lateral to the spinous process and contact is made with the posterior tubercle of the transverse process. The majority of the more recent workers have abandoned all these methods except the supraclavicular route. Labat [11] described a technic by which the needle was inserted supraclavicularly and pointed in three directions in order to reach the plexus at three points. (Fig. 5.) Lundy]12] described a three-needle technic as originated by Knight whereby the trio of needles are placed one above the other on the first rib at about .5 cm. distance on a parallel line anteroposteriorly beginning at the junction of the inner and middle third of the clavicle and one fingerbreadth above it. (Fig. 6.)

Difficulties with These Methods. All the foregoing methods were characterized by frequent failures in the writers' hands. Either

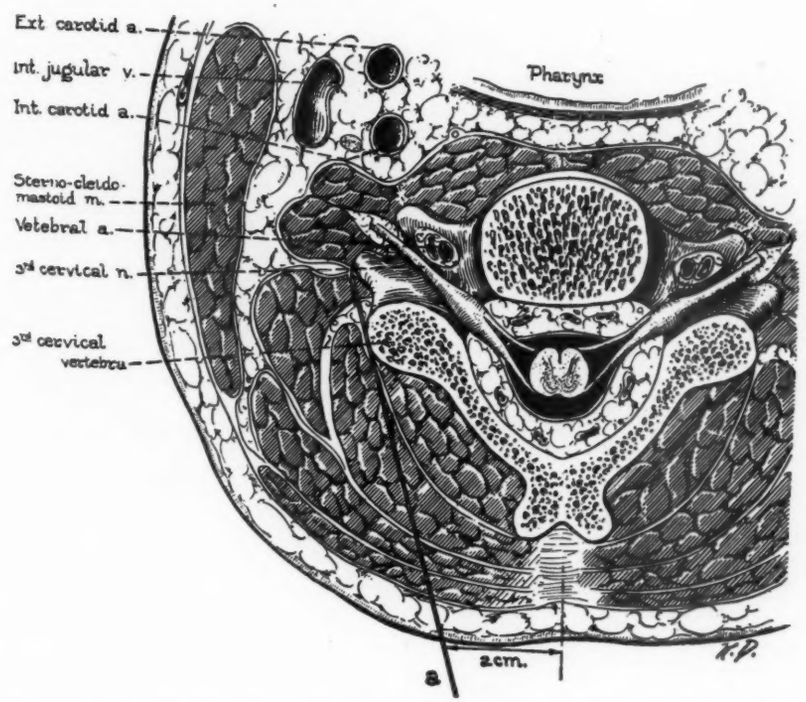

FIG. 4. Cervical plexus block by the posterior route which may be employed for brachial plexus block at appropriate levels. Cross section of the neck at level of C3 showing direction of the needle (*a*) inserted at a point 2 cm. from the midline of the back of the neck. (From: LABAT, G., Regional Anesthesia, Its Technique and Clinical Application. Philadelphia, 1928. W. B. Saunders Co.)

anesthesia was not initiated at all, or if it was, all too frequently a "wearing off" of the anesthesia occurred before the operation was finished and resort to general anesthesia was rendered imperative. Reblocking was more difficult on account of the impediments produced by the surgical drapes, and in addition the nervous state of the patient often precluded the attempt as he was unwilling to cooperate on account of the pain being experienced in the part. For these reasons we believed that a method should be developed by which we could be certain of the production of anesthesia in the arm, in which there would be no question of its outlasting the operative procedure, and in which motor power usually would be retained by the patient. With these thoughts in mind a method of brachial block was employed using 1 or 2 per cent [*13*] nesacaine* (chloroprocaine) and employing a new reblocking technic which did not interfere with the operative procedure and could be done with ease and facility.

* Supplied by Wallace & Tiernan, Inc., Maltbie Laboratories Division, Belleville, N. J.

Moore and Bonica state that since the introduction of long-acting pontocaine the need for continuous brachial block is no longer present except in rare instances, and we now subscribe to this view since the introduction of the reblocking technic with nesacaine.

ANATOMY OF BRACHIAL PLEXUS

To induce blockade of the brachial plexus and to insure dependability of the block, it is important to visualize some essential points in anatomy. The plexus is composed (Fig. 7) of the anterior primary divisions of the last four cervical nerves (C_5, 6, 7 and 8) and the first dorsal nerve (D1). From these five roots the nerves from C_5 and 6 join to form the upper trunk. The fibers from C7 form the middle trunk and those from C8 and D1 form the lower trunk. Each of these three trunks then produces branches (anterior and posterior). (Fig. 8.) All the posterior branches join to form the posterior cord. The anterior branches from the upper and middle trunks form the lateral or outer cord and the anterior branch of the lower trunk forms the medial or lower cord.

Thus three cords result and these in turn give off the five main nerves of the upper extremity—the musculocutaneous, the median, the ulnar, the radial and the axillary. Thus the plexus may be said to begin with five nerves (C5, 6, 7, 8 and D1) and to end with five nerves

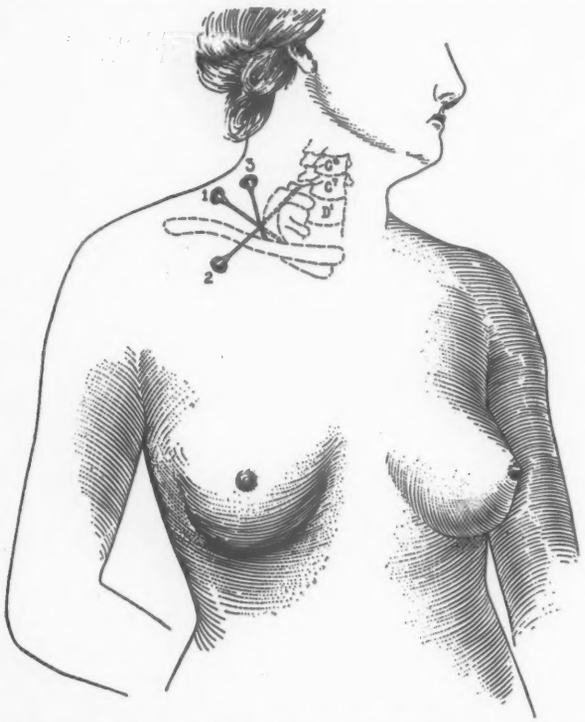

FIG. 5. Brachial plexus block by the supraclavicular route. The three directions of the needle as originally described by Labat. (1) Aims at the first rib; (2) at the transverse process of C6; (3) at the lateral margin of the first rib behind the clavicle. (From: LABAT, G. Regional Anesthesia, Its Technique and Clinical Application. Philadelphia, 1928. W. B. Saunders Co.)

with its intermediate portions in sets of three (three trunks, three sets of anterior and posterior branches, and three cords) [*14*]. It must be constantly borne in mind that the plexus is surrounded on all sides by muscle and fascial sheaths and is enveloped by them. As previously stated, the plexus originates from the anterior primary divisions of C5, 6, 7, 8 and D1. The roots come off the spinal cord at these levels, pass through their respective intervertebral spaces and emerge peripherally across the transverse processes. The processes in the cervical region are cup shaped and consist of an anterior tubercle and posterior tubercle with a gutter for the nerves between them. As each nerve passes off its respective transverse process, it is enclosed first by a sheath of fascia uniting the anterior and posterior tubercles, thus forming a tunnel through which the nerve passes. After emerging from this tunnel each nerve is enclosed by the scalene muscles (Fig. 9) as they descend toward the first rib, the scalenus anticus originating from the anterior

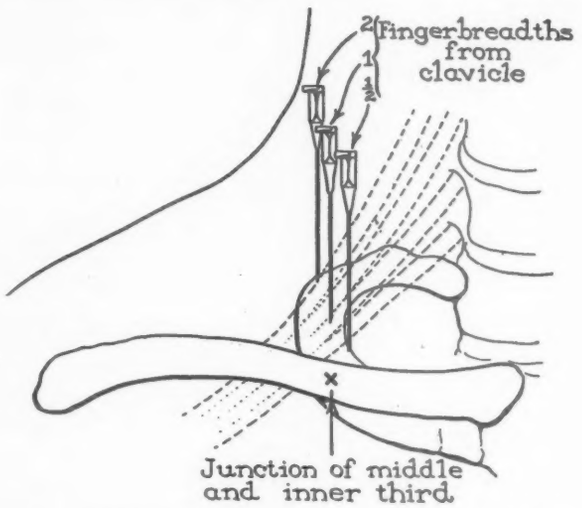

FIG. 6. Brachial plexus block by the method of Knight. The plexus is dotted to show its relationship to the clavicle and the first rib. Injection is made from the first rib to skin through each needle as it is withdrawn to infiltrate the region through which the plexus passes. (From: LUNDY, J. S. Clinical Anesthesia. Philadelphia, 1942. W. B. Saunders Co.)

tubercles and the scalenus medius from the posterior tubercles. The latter muscle is inserted on the first rib posterior to the groove on the rib made for the passage of the plexus and the subclavian artery. The scalenus anticus muscle originates from the anterior tubercles of the transverse processes of C4, 5 and 6. It takes a downward direction and is inserted by a narrow tendon into the scalene tubercle of the first rib. In its upper part the muscle lies in contact with the plexus, but at the point of its insertion into the first rib it is separated from the plexus by the intervention of the subclavian artery which had arched out of the thorax to cross the first rib and become the axillary artery. Thus the brachial plexus as it crosses the first rib lies between the scalenus anticus and the scalenus medius. The subclavian artery also lies between these two muscles. It is of paramount importance to bear in mind that the plexus lies *lateral* to the artery although there are occasional variations in the relationship of the artery to the tendon of the scalenus anticus [*15*]. The plexus is

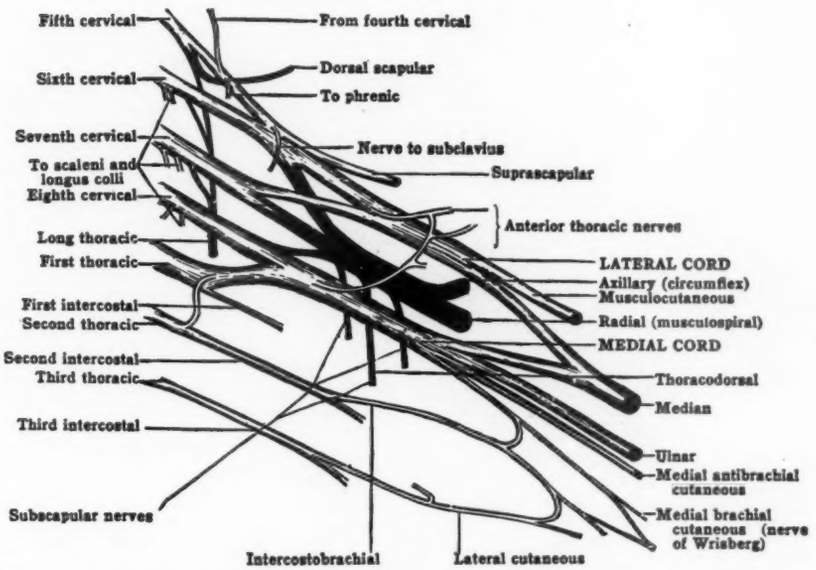

FIG. 7. Roots, trunks, branches and cords of the brachial plexus. The posterior divisions and cord of the plexus are darkly shaded. (From: MERRITT, H. H., METTLER, F. A. and PUTNAM, T. J. Fundamentals of Clinical Neurology. Philadelphia, 1947. Blakiston Co.)

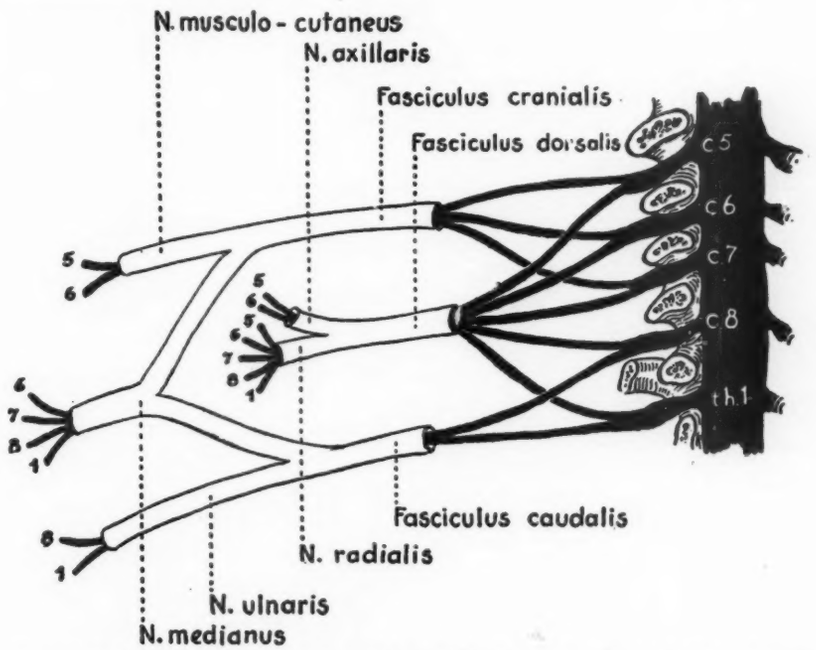

FIG. 8. Schematic representation of brachial plexus showing relation of roots to nerves. (From *M. Times*, 85: 478, 1957.)

enclosed by a fascial sheath. (Fig. 10.) This sheath covers the plexus in three planes and consists: (1) anteriorly of the superficial layer of the deep cervical fascia, (2) medially of the posterior sheath of the scalenus anticus muscle, and (3) laterally of the anterior sheath of the scalenus medius and posticus.

Thus the anesthetic solution must be deposited into this space between the fascial layers in order to reach the plexus. If deposited outside this space, anesthesia will not be produced.

Macintosh and Mushin [*16*] emphasized the anatomical relationship of the plexus to the

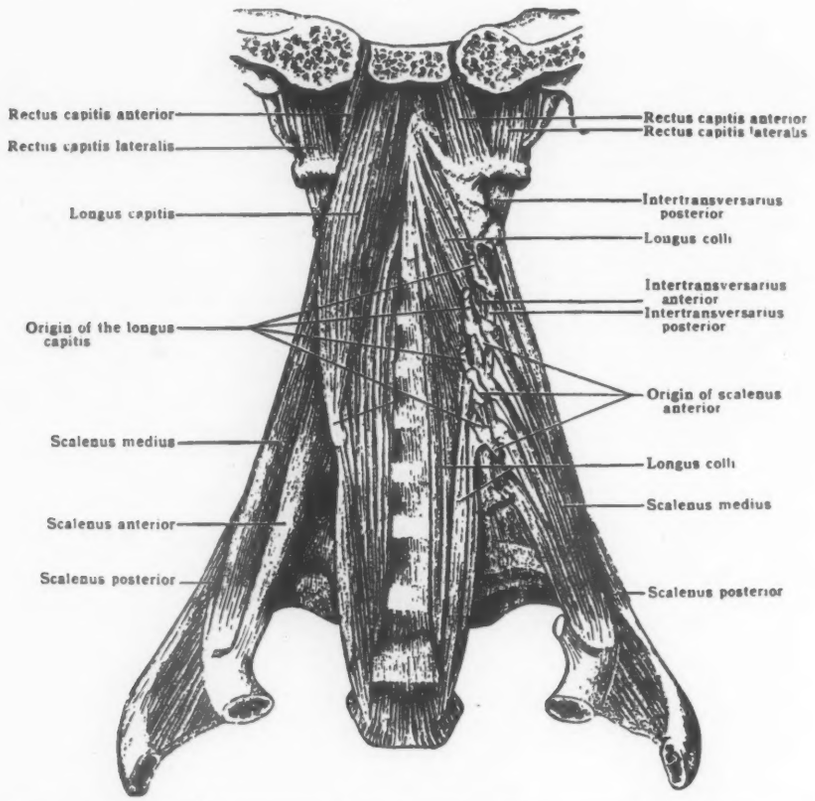

FIG. 9. The origin and course of the scalenus muscles. (From: SCHAEFFER, J. P. Editor. Morris' Human Anatomy, 11th ed. New York, 1953. Blakiston Division, McGraw-Hill Book Co.)

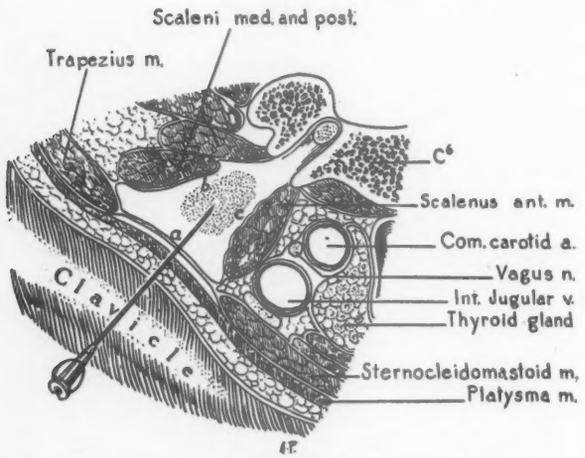

FIG. 10. Cross section (half diagrammatic) of the supraclavicular region illustrating the pyramidal extension of the cervical fascia investing the brachial plexus; (*a*), (*b*) and (*c*) are the walls of the pyramid within which the injected fluid is shown. (From: LABAT, G. Regional Anesthesia, Its Technique and Clinical Application. Philadelphia, 1928. W. B. Saunders Co.)

subclavian artery. Their method of locating the plexus (by first palpating the subclavian artery as it crossed the first rib and inserting a needle lateral to the artery and in close contact with it so that the needle moved with the pulsations of the artery, and construing as *prima facie* evidence that the needle of necessity must be in the immediate vicinity of the plexus), induced one of us (F. P. A.) to carry this method a step further and adapt it to a continuous principle [*1*].

Accordingly, our method of brachial plexus block depends essentially on the certain location of the needle in close proximity to the plexus (as described by MacIntosh and Mushin) and on the employment of a dilute and relatively non-toxic solution of nesacaine in order that a "flooding" of the area may render blockade of the plexus more certain instead of depending entirely on the accurate location of the needle in the substance of the plexus which has in the past proved so unreliable. Previously it was considered essential to avoid the subclavian artery and seek contact with the plexus. We, in effect, avoid the plexus and seek the artery, although an unsought

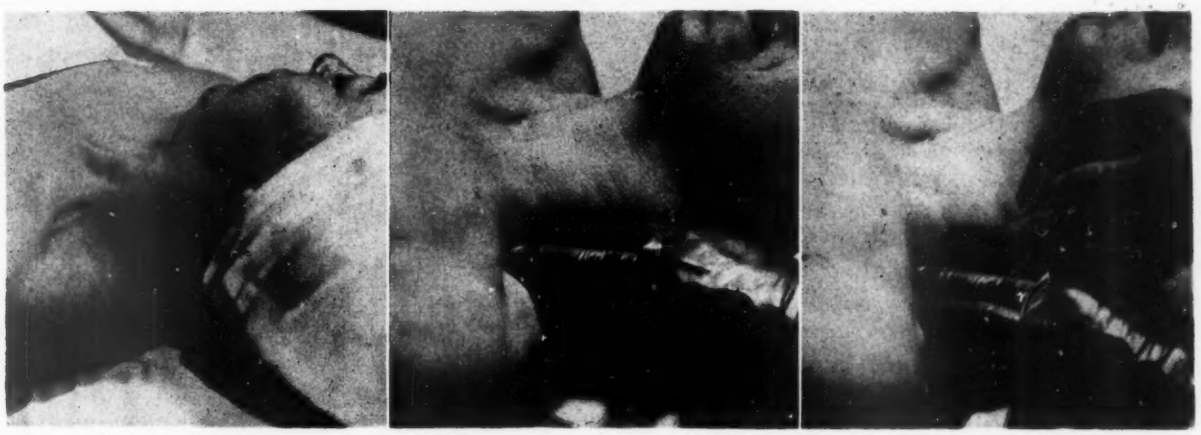

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FIG. 11. The sternal and clavicular heads of the sternocleidomastoid muscle are made evident by having the patient lift his head off the table with the head in 30 degree rotation. The scalenus anticus muscle may be palpated at the lateral border of the body of the sternocleidomastoid muscle.

FIG. 12. Palpation of the subclavian artery and the first rib at the above-head position. The brachial plexus lies lateral to the artery as they cross the first rib.

FIG. 13. With the middle finger of the left hand palpating the subclavian artery and the first rib, the needle is directed lateral to the artery to contact the rib. The hands of the operator are then removed from the area and the "pulsations" of the needle are noted as it transmits the pulsations of the artery. If the needle pulsates vigorously, injections of nesacaine are made without moving the needle.

paresthesia when obtained is seized upon and the needle is retained *in situ*.

PROCEDURE

The mid-point of the clavicle is determined by careful measurement. The insertion of the scalenus anticus is also palpated according to the method of Taylor as described by Moore [*17*]. This consists of having the patient lift his head 2 inches off the table while in the dorsal recumbent position and turn the head to the side opposite the block. (Fig. 11.) This position puts a strain on the neck muscles. The clavicular head of the sternocleidomastoid muscle is palpated, and by going slightly lateral to the edge of this muscle the anterior scalene can be palpated. The subclavian artery is lateral to the scalenus anticus and the brachial plexus is lateral to the artery. The importance of palpating the subclavian artery as a guide to the plexus is the key to the procedure. The other steps are ancillary to it. Following the exact determination of these landmarks which are usually found at the mid-point of the clavicle and 2 cm. above it, the first rib is palpated at the same time. In thin patients the rib is easily felt just beneath the skin and at the mid-point the clavicle is in a direction almost anteroposterior and not circular as often conceived by the neophyte. With these landmarks firmly established, the operator stands at the head of the patient. (Fig. 12.) We have found after lengthy trial and experience that it is easier to perform brachial plexus block by standing at the head of the patient with the head in moderate flexion and in the midline, the arm being close to the side. Palpation of the subclavian artery and the first rib is rendered much easier by this position because it relaxes the neck muscles of the patient and makes the structures readily felt; in addition, the operator is able to apply pressure to the parts by employing some of his body weight against his palpating fingers which in turn does not induce fatigue in the fingers from strain. The fingers of the left hand (in right-handed operators) are used for right or left side block. The index finger palpates the pulsations of the subclavian artery and at the same time the bony structure of the first rib. (Fig. 12.) Moving the finger slightly lateral to the artery and palpating the rib, the needle in the right hand is directed just medial to the palpating finger, and at a variable depth (usually 3 to 4 cm.) the rib is contacted. (Fig. 13.) Both hands are withdrawn and the oscillations of the needle observed as it is "rocked" by the pulsations of the subclavian artery. If the

oscillations are pronounced, the procedure for locating the plexus is finished. If not pronounced, the point of the needle is moved slightly medial until oscillations are pronounced. If the plexus is contacted by the needle paresthesias will be established in the form of shooting pains along the course of the plexus into the arm and hand. These paresthesias are helpful in locating the plexus and give further assurance of its proximity; however, they are not essential to success by this technic. If nesacaine is injected at this location in sufficient quantity, a successful infiltration of the plexus will result. The operator's hands are now removed from the needle; and if the needle is in contact with the subclavian artery, it will move with the pulsations of the artery. It is essential that these pulsations be observed; otherwise failure to be in the immediate vicinity of the plexus in the absence of paresthesias may result in not obtaining anesthesia. When the position of the needle is determined to be correct and after careful aspiration to ascertain that the needle is not in a blood vessel, injection of nesacaine is performed. It has been observed that 1 per cent procaine does not produce motor paralysis, whereas 2 per cent does affect motor nerves [*18*]. The same was found true as regards nesacaine; and for this reason and because less concentration has less toxicity, the 1 per cent solution was used in the series when it was desired to retain motor power in the arm. Usually 35 cc. (without adrenalin) are injected and the onset of anesthesia may be expected within ten to fifteen minutes. Large amounts of nesacaine are tolerated well by the average patient [*19*].

A saline glucose infusion should be administered in every case and 0.2 per cent pentothal® should be ready to combat any possible toxic effects. So far, no need for the barbiturate has been seen using the 1 per cent or 2 per cent solution of nesacaine. The average duration of anesthesia was one and a half hours, the longest case being eight hours and the shortest one hour. The average amount of solution varied from 35 cc. used in the shortest procedure to 100 cc. used in the longest. During a long operation, if the block appeared to be wearing off, the needle was reinserted and 35 cc. of 1 per cent nesacaine injected. Some tachyphylaxis was observed here, as the second injection did not last as long as the first. In the longer operations it was necessary to repeat the injections several times. This was easily done by the "above-head" position of the anesthesiologist and was unnoticed by the operating surgeons. Good sensory anesthesia was obtained in all but two of the cases. The procedures varied from open reduction operations on bones of the forearm, arm and shoulder to repair of a divided median nerve and palmaris longus tendon. For operations on the shoulder, an additional injection may be made at the fourth cervical transverse process to block the C_4 nerve which supplies the skin of the shoulder; or on withdrawing the needle to just beneath the platysma and injecting 5 cc. of nesacaine, the descending branch of the cervical plexus which supplies the skin of the shoulder region will be blocked [*11*]; or infiltration of the skin area above the clavicle and acromion and circularly about the axilla along its thoracic surface may be carried out to block the superficial branches of the cervical plexus.

The majority of patients returning to bed appeared to have no deleterious effects. The physical economy of these patients apparently has been but slightly altered by their anesthesia and operation. Many expressed a desire for food and required very little sedation. Those with plaster casts on the arm and chest were able to sit up and move about freely immediately after operation.

Therapeutically, block of the brachial plexus has been used in cases of embolism of the upper extremity occurring as a result of cardiac disease. Its use in peripheral vascular accidents in the upper extremity is based on the distribution of the sympathetic components of the plexus which after leaving their cells of origin accompany the nerves of the brachial plexus and are distributed to the blood vessels and sweat glands of the limb. Thus block of the brachial plexus produces not only a somatic but also a sympathetic paralysis producing a rise in skin temperature and a dryness of the skin. In arterial occlusion there is a relief of pain and vasodilatation of collaterals which is conducive to better circulation in the occluded extremity.

RESULTS

We found our results better than formerly with this method of blocking the brachial plexus. The above-head position* facilitated

* We first saw this position in a motion picture by J. J. Bonica, M.D.

TABLE 1
BRACHIAL PLEXUS BLOCK (FIVE-YEAR PERIOD)

Surgical Condition	No. of Cases	Duration (hr.)	Amount of Nesacaine (cc.) (1 or 2%)	Results		
				Success	Failure	Partial
Fractures (of long bones, wrist, hand)	192	1–4	35–75	177	14	1
Skin grafts	48	1½–2½	35–50	44	2	1
Repair of tendons and nerves	84	3–8	35–100	76	6	1
Manipulations	20	1	35	18	1	..
Repair of lacerations	104	1–2	35–50	98	5	1
Amputations	74	1–2½	35–60	67	8	1
Incision and drainage	202	1	35	185	14	2
Revisions	160	1–2	35–60	145	12	2
Foreign bodies	144	1–2	35–60	131	10	2
Crush injuries	120	1–3	35–100	115	8	1
Therapeutic	14	.....	20–50	12	2	1

insertion of the needle, and the utilization of the principles of Macintosh and Mushin rendered the placement of the needle more accurate. We have increased the success of our blocks from 75 to 92 per cent. With more experience we will probably obtain even better results. Nesacaine has been a valuable agent in our hands. Properly deposited near the plexus, it will produce a block. Our failures have been due to faulty technic, or excessive haste or both. Blockade of the brachial plexus takes time to become effective and this must not be lost sight of if the anesthesiologist wishes to have his efforts rewarded by an impressive percentage of successes. Table 1 indicates the types of operations in which brachial plexus block was utilized, with the results obtained. There were no complications as regards toxicity; there were five cases of pneumothorax.

SUMMARY AND CONCLUSIONS

Brachial plexus block was performed in 1,162 cases, utilizing the above-head position and the principles of proper placement of the needle as described by Macintosh and Mushin. By these means our successful blocks were increased from 75 to 92 per cent. The history of the method and the anatomy involved are described. The technic is recommended for operations on the upper extremity and for therapeusis in promoting increased circulation in the arm in cases of ischemia.

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The Clinical Trial of Streptomycin Pantothenate in the Treatment of Soft Tissue Infections*

RUPERT A. LACAILLE, M.D. AND AARON PRIGOT, M.D., *New York, New York*

From the Department of Surgery of Harlem Hospital, Department of Hospitals, New York City.

THE role of streptomycin alone and in combination with penicillin in the treatment of soft tissue infections has been well documented. Damage to the eighth cranial nerve, associated with prolonged or intensive streptomycin therapy, is a serious consideration and has limited the usefulness of this antibiotic to infections in which its possible ototoxic effect was outweighed by the gravity of the illness.

In experimental studies in 1955, Keller [1,2] and his associates showed that the pantothenic acid salt of streptomycin considerably reduced the acute toxicity in white mice and in rats. Chronic toxicity in cats was suppressed for weeks when 20 per cent streptomycin pantothenate was administered in addition to streptomycin sulfate.

In a clinical evaluation of its effectiveness in pulmonary tuberculosis [3] at Harlem Hospital, streptomycin pantothenate 20 per cent, dihydrostreptomycin 80 per cent, equivalent to 1 gm. of dihydrostreptomycin base, was used over a period of six months. Although the patients receiving this medication had previously suffered severe side reactions with streptomycin and dihydrostreptomycin, no such toxicity developed with the streptomycin pantothenate preparation.

This communication deals with the use of streptomycin pantothenate, in conjunction with surgery, in the treatment of 116 patients with soft tissue infections. Some of the patients were hospitalized, but many could be managed on an ambulatory basis. The antibiotic decreased the incidence of surgical intervention and in many instances the procedures were less extensive than ordinarily performed in similar cases. Table 1 lists the types of infections involved in this study.

TABLE 1
PATIENTS WITH SOFT TISSUE INFECTIONS TREATED WITH DIDROTHENATE

Diagnosis	No. of Patients
Cellulitis, with or without lymphangitis	27
Abscess:	
Axillary	13
Inguinal (non-venereal)	12
Felon	10
Infected lacerations:	
Upper extremity	10
Lower extremity	4
Chest	7
Acute epidydimitis	7
Human bite	5
Infected arm	5
Infected leg	5
Infected foot	9
Infected chin	1
Infected hand	1
Total No. of patients	116

The dose schedule in these cases varied. All ambulatory patients received 1 gm. of didrothenate intramuscularly daily. For hospitalized

* This investigation was supported, in part, by a grant from the Lederle Laboratories Division of the American Cyanamid Company, Pearl River, New York. The trade name of this company for the combination of dihydrostreptomycin sulfate and dihydrostreptomycin tripantothenate, employed in this study, is didrothenate.

1 2

FIGS. 1 and 2. Case II. (10/29/56). Infection of the third finger of the right hand resulting from a human bite. With streptomycin pantothenate therapy and incision and drainage the infection resolved and the wound healed in seventeen days.

patients the dosage was 0.5 gm. three or four times daily, depending on the severity of the infection. The average duration of treatment for the ambulatory patients was seven days, while the more seriously ill hospitalized patients remained under treatment for an average period of twenty-one days. Even this longer course produced no evidence of allergenic or toxic attributes in the medication; the injection was not painful and in no instance was the antibiotic withdrawn before completion of therapy.

The following four patients are typical of those treated in the hospital. In all instances the infection cleared rapidly, permitting definitive surgery when indicated.

CASE REPORTS

CASE I. L. S., a thirty year old man, was admitted to the hospital on October 15, 1956, with a three week history of an ulceration of the anteromedial aspect of the left leg. This ulcer had arisen spontaneously as a pinpoint defect which progressively enlarged. On admission the ulcer measured 7 cm. in diameter.

The patient was placed on a schedule of streptomycin pantothenate, 500 mg. three times a day for four weeks, during which time the cellulitis and inflammation subsided, leaving a healthy granulating surface.

Culture of the exudate from the ulcer revealed beta streptococcus and staphylococcus aureus.

On December 18, 1956, a skin graft was applied to cover the defect and on February 25, 1957, the patient was discharged as completely healed.

CASE II. J. W., a thirty-two year old man, sustained a human bite of the third finger of the right hand and subsequently a secondary infection developed. On admission to the hospital on October 27, 1956, the finger was painful, swollen and macerated. (Figs. 1 and 2.) A diagnosis of cellulitis with tenosynovitis was recorded.

S. aureus was identified in a culture of the exudate from the infected area.

Streptomycin pantothenate was prescribed, 500 mg. four times daily, and the patient remained on this medication for sixteen days.

Incision and drainage was performed on October 28th and the patient was discharged on November 13th, the infection having completely resolved and the wound healed.

CASE III. P. H., a forty-one year old man, was hospitalized on November 7, 1956, for osteomyelitis of the left great toe. (Fig. 3.)

In bacteriological studies S. aureus was isolated as the infecting organism.

Streptomycin pantothenate therapy, as 500 mg. three times daily, was continued for a total of twenty-six days.

The inflammatory condition gradually subsided (Fig. 4) and the patient had an uneventful recovery and was discharged on December 4, 1956.

CASE IV. F. P., a sixty-eight year old man, was admitted to the hospital on October 26, 1956, with an abscess of the left foot, which on bacteriological culture revealed S. aureus and Bacillus proteus.

On a course of treatment with streptomycin pantothenate, 500 mg. three times daily for thirty days, the inflammatory process receded and the

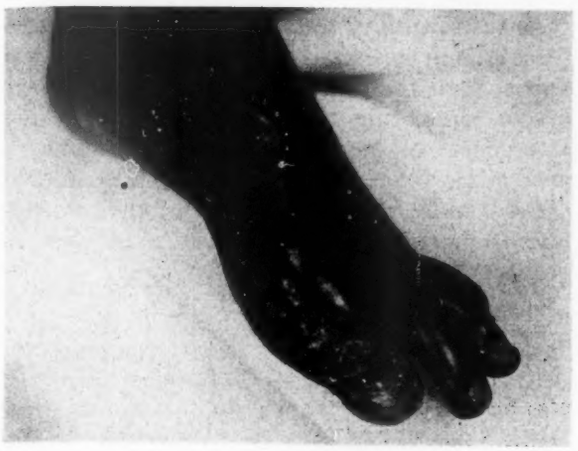

FIG. 3. Case III. (11/7/56). Osteomyelitis of the left great toe prior to antibiotic therapy.

FIG. 4. Case III. (12/4/56). Healing of lesion after twenty-six days of streptomycin pantothenate treatment, no surgery being required.

wound healed. The patient was discharged on February 8, 1957.

BACTERIOLOGY

When exudates were available from the sites of infection in the patients under this study, these were cultured and the following microorganisms were recovered: S. aureus, 17 strains; Beta streptococcus, 3 strains; Escherichia coli, 3 strains; Staphylococcus albus, 1 strain; Paracolon bacillus, 1 strain; and B. proteus, 1 strain.

In susceptibility tests two strains of E. coli and one strain each of S. albus and S. aureus were found resistant to both streptomycin and streptomycin pantothenate. The remainder of the isolated organisms were susceptible to both antibiotics. Of the twenty-two susceptible strains, six were more sensitive to the streptomycin pantothenate than to streptomycin. In no case were the organisms cultured more sensitive to streptomycin sulfate.

The antibacterial action of streptomycin is enhanced by the simultaneous administration of penicillin. To determine whether such a synergism between didrothenate and penicillin can be demonstrated clinically, twenty patients with soft tissue infections were treated with this antibiotic combination, as summarized in Table II.

The dose schedule employed was 1 gm. of didrothenate and 300,000 units of penicillin administered intramuscularly each day, the average duration of medication being six days. All patients responded well, completing the prescribed course with no allergic or toxic manifestations. The injection of the two antibiotics was not more uncomfortable than a similar dose of penicillin alone.

The established synergism between streptomycin and penicillin appears to obtain also when the latter antibiotic is administered simultaneously with didrothenate.

TABLE II
PATIENTS WITH SOFT TISSUE INFECTIONS TREATED WITH DIDROTHENATE AND PENICILLIN

Diagnosis	No. of Patients
Cellulitis of the hand with lymphangitis	5
Felon	3
Axillary abscess	3
Human bite of the hand	2
Infected lacerations:	
Forearm	4
Face	2
Chest wall	1
Total No. of patients	20

CONCLUSIONS

1. The pantothenate of streptomycin, used alone or in conjunction with penicillin in the treatment of soft tissue infections, produced an excellent therapeutic response in all cases.

2. The pantothenate of streptomycin eliminates the toxic and side reactions associated with streptomycin and dihydrostreptomycin and in no case in this series was the medication withdrawn before the completion of treatment.

3. The use of the antibiotic results in fewer patients being subjected to surgery, the employment of surgical procedures of lesser magnitude, and a decrease in morbidity.

4. The microorganisms recovered were more susceptible to the pantothenate of streptomycin than to streptomycin sulfate. The possibility of the emergence of strains resistant to streptomycin is thereby decreased.

5. The inhibitory effect of the pantothenate of streptomycin on both gram-positive and gram-negative organisms, the high level of patient tolerance and clinical response, and the absence of toxicity, make this new antibiotic a valuable adjunct in the management of soft tissue infections.

SUMMARY

Didrothenate was the antibiotic employed in the treatment of 116 patients with soft tissue infections, some of whom were managed on an ambulatory basis. Surgical intervention was required in fewer instances and was usually of lesser magnitude than ordinarily employed in similar cases. The intramuscular administration of the antibiotic was acceptable to the patients and the therapeutic response to this medication was excellent.

In susceptibility tests on the microorganisms recovered in this study more strains were found sensitive to the didrothenate than to streptomycin, indicating that the possibility of the emergence of resistant bacterial strains is decreased. None of the organisms recovered proved more sensitive to streptomycin sulfate than to the streptomycin pantothenate preparation.

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The Inhibition of Clotting by Chlorophyllin

JOSEPH M. MILLER, M.D., DEBORAH A. JACKSON, B.S. AND CHARLES S. COLLIER,
Fort Howard, Maryland

From the Surgical Service and General Medical Research Service of the Veterans Administration Hospital, Fort Howard, Maryland.

DURING an investigation of the properties by which the water-soluble derivatives of chlorophyllin increased the rate of healing in infected wounds, it was noted that sodium-copper chlorophyllin inhibited the conversion of fibrinogen to fibrin by thrombin [*1*]. Detailed investigations were undertaken to determine the quantitative aspect of the inhibition, the effect of varying the order of addition of fibrinogen, thrombin, and chlorophyllin, if lysis of clots was produced by chlorophyllin, and whether or not the results obtained were due to the effect of copper as shown by the use of sodium-iron chlorophyllin on the formation of fibrin clots.

MATERIALS

Bovine Fibrinogen (*Armour*). The fibrinogen was weighed and was ground in a mortar with a small amount of borate buffer to make an 0.25 per cent solution unless otherwise indicated. The solution was made just before it was used.

Thrombin, Hemostatic Globulin (*Lederle*). Thrombin, hemostatic globulin, four per cent in an 0.05 normal acetate buffer solution. An 0.05 N acetate buffer solution was made by dissolving 0.68 gm. of sodium acetate in 100 ml. of distilled water. A 4 per cent stock solution of the thrombin in the acetate buffer solution was prepared. The reaction was adjusted to a pH of 5.8 with hydrochloric acid. Not more than 100 ml. of the solution was prepared at one time since it had a tendency to become contaminated with molds. The solution was stored in a refrigerator when it was not being used. An 0.8 per cent solution of the stock preparation was made by dilution with the borate buffer solution at a pH of 7.2 to make the fibrin clots. The solution was prepared just before it was used.

Borate Buffer Solution. The borate buffer solution was made as follows: Boric acid, 11.1 gm., was dissolved in a small amount of warm distilled water. Sodium borate ($Na_2B_4O_7.10H_2O$), 7.0 gm., and 9.0 gm. of sodium chloride were added and dissolved. Distilled water to make 1,000 ml. was added. The solution was adjusted to a pH of 7.2 to 7.4 with hydrochloric acid.

TABLE 1
EFFECT OF DIFFERENT DILUTIONS OF CHLOROPHYLLIN ON VARIOUS CONCENTRATIONS OF FIBRINOGEN USING A STANDARD SOLUTION OF THROMBIN

Per cent Chlorophyllin 0.1 ml.	Fibrinogen 0.125 Per cent (50 mg./40 ml.) 0.4 ml.	Fibrinogen 0.25 Per cent (50 mg./20 ml.) 0.4 ml.	Fibrinogen 0.5 Per cent (50 mg./10 ml.) 0.4 ml.
0.30	−	−	−
0.15	−	−	±
0.075	−	±	+
0.037	±	+	+
0.018	+	+	+
0.009	+	+	+
0.0045	+	+	+
0.0023	+	+	+

NOTE: + = Solid clot present.
± = Loose clot present.
− = Clot not present.

*Solution of Sodium-Copper Chlorophyllin.** An 0.3 per cent solution of sodium-copper chlorophyllin was made in a borate buffer. The solution was made just before it was used.

METHOD

Chlorophyllin, 0.1 ml. of the different dilutions, was added to 0.4 ml. of a 0.125, a 0.25, and a 0.5 per cent solution of fibrinogen and the solutions were mixed. Thrombin, 0.1 ml. of an 0.8 per cent solution, was added imme-

* The sodium-copper chlorophyllin was supplied by the Rystan Company, Mount Vernon, New York.

TABLE II
EFFECT OF CHANGING THE ORDER OF ADDITION OF THE REAGENTS

Per cent Chlorophyllin	a. Chlorophyllin b. Fibrinogen c. Thrombin	a. Thrombin b. Chlorophyllin c. Fibrinogen	a. Fibrinogen b. Chlorophyllin c. Thrombin	a. Fibrinogen b. Thrombin c. Chlorophyllin
0.30	−	−	−	±
0.15	±	±	±	±
0.075	±	±	±	±
0.037	±	±	±	+
0.018	+	+	+	+
0.009	+	+	+	+
0.0045	+	+	+	+

NOTE: + = Solid clot present.
± = Loose clot present.
− = Clot not present.

diately. Observation for clotting was made at two, five, ten, and fifteen minutes. It was usually complete at about two minutes and the results were recorded at fifteen minutes. Observation for lysis was made at two, five, ten, and fifteen minutes. It was usually complete at about ten minutes and the results were recorded at fifteen minutes.

The results indicated that chlorophyllin inhibited the conversion of fibrinogen to fibrin by thrombin. (Table I.) The inhibition was dependent upon the strength of the solution of chlorophyllin and the concentration of fibrinogen since the amount of thrombin used was standard throughout the experiment.

A change in the order of addition of the reagents conceivably could change the results. Chlorophyllin, 0.1 ml. of the various dilutions, 0.4 ml. of a 0.25 per cent solution of fibrinogen, and 0.1 ml. of an 0.8 per cent solution of thrombin were mixed as indicated in Table II. The results were essentially the same.

Likewise, chlorophyllin might produce lysis of fibrin clots rather than inhibition of their formation. Fibrinogen, 0.4 ml. of a 0.25 per cent solution, and 0.1 ml. of an 0.8 per cent solution of thrombin were mixed and a clot was formed. The clots were physically broken up and chlorophyllin, 0.1 ml. of the various dilutions, was added. The addition of chlorophyllin to fibrin clots left untouched gave essentially the same results. (Table III.)

The use of sodium-iron chlorophyllin* with bovine fibrinogen and thrombin gave results similar to sodium-copper chlorophyllin so the ionic effect of copper and iron could be eliminated as a cause of the inhibition of the formation of fibrin clots. When the sodium-iron chlorophyllin was used with bovine fibrinogen and thrombin (Upjohn), a similar pattern was obtained.

* The sodium-iron chlorophyllin was supplied by the Rystan Company, Mount Vernon, New York.

TABLE III
EFFECT OF ADDING CHLOROPHYLLIN AFTER THE FORMATION OF FIBRIN CLOTS

Per cent Chlorophyllin	Fibrin Clot Broken Up Physically	Fibrin Clot Left Untouched
	Type of Clot	Type of Clot
0.30	±	±
0.015	±	±
0.075	±	+
0.037	+	+
0.018	+	+
0.009	+	+
0.0045	+	+

NOTE: + = Solid clot present.
± = Loose clot present.

COMMENT

The inhibition by chlorophyllin of the polymerization of fibrinogen to fibrin by thrombin may be important in the treatment of inflammation by enhancing the local action of the defense mechanisms of the host and of the antibacterial drugs. Most antibacterial drugs are bacteriostatic rather than bactericidal. To obtain better results in the treatment of infec-

tions, greater amounts of the immune humoral forces or of the antibacterial drugs must be delivered at the site of the infection. The achievement of these goals requires that a modification of the chemical environment in the area of inflammation must be produced, perhaps by the removal of fibrin. Fibrin is formed in the limiting membrane about such an area, and, in it, from fibrinogen, diffusing from the blood stream, through the action of thrombin liberated from disintegrated blood platelets. Modification of the environment may be produced by the use of chlorophyllin to inhibit the conversion of fibrinogen to fibrin. The presence of fibrin is detrimental to the regression of the infection for many reasons.

Fibrin may provide a chemical or mechanical barrier to phagocytosis. Coagulase positive strains of staphylococci clot blood plasma [4]. The fibrin coats the bacteria and inhibits phagocytosis [7]. Phagocytosis, which is an important part of the defense of the host, is best effected on a surface where leukocytes can trap bacteria against an opposing surface such as the wall of the tissue involved or other leukocytes [7–9]. Surface phagocytosis is relatively inefficient in open cavities such as those formed by the peritoneum, the pleura, the pericardium, and the meninges [9]. Leukocytes are not good phagocytes in fluid [9]. When an adequate supply of oxygen is lacking, the leukocytes become non-motile and lose their power of phagocytosis [6]. Fibrin increases the viscosity of edema fluid and the area of inflammation swells. Thrombi are deposited in the arteries, capillaries, veins and lymphatics. The combination of edema and obstruction of the blood vessels and of the lymphatic vessels leads to hypoxia or anoxia.

Hughes [2,3] has demonstrated that the wall of fibrin about the site of inflammation is remarkably selective in permeability. Under pressure, albumin will filter through but globulin, containing antibodies, will not do so. Some bacterial toxins will slowly diffuse through outwardly although most products of such origin will not do so. Bacteria are restrained but polymorphonuclear neutrophilic leukocytes pass readily.

In the presence of an open wound the local application of chlorophyllin may help considerably in controlling the inflammatory reaction. The inhibition of clotting of fibrin will do much to alleviate conditions which, if they are not checked, will promote the severity of the inflammation.

SUMMARY

The water-soluble derivatives of chlorophyllin had the ability to inhibit the formation of fibrin clots when thrombin was added to fibrinogen. Apparently, a direct relationship was present between the amount of chlorophyllin and the concentration of fibrinogen in the reaction. Chlorophyllin did not cause the solution of fibrin clots after they were formed.

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Chemotherapeutic Management of Granulocytic Leukemia

JOHN R. SAMPEY, PH.D., *Greenville, South Carolina*

From the Chemistry Department, Furman University, Greenville, South Carolina.

AN increasing number of investigations are being made on the management of granulocytic leukemia with chemotherapeutic agents. In the present study, of the 649 patients who had been treated, 575 had chronic, sixty-seven acute, and seven undifferentiated granulocytic leukemia. Table I shows that 304 of these responded to chemotherapy but this is not the entire story, for twelve of the forty-five investigations recorded no data on the number of patients having remissions. Myleran,® TEM, ACTH and cortisone have called forth the largest number of publications, but radiophosphorus has been administered to the largest number of patients (Table II), and 6-MP is the agent of choice of several investigators [28].

COMMENTS ON CHEMOTHERAPEUTIC AGENTS

Myleran. Reports on the management of chronic granulocytic leukemia are as complete as those on the chemotherapeutic treatment of any type of leukemia [46]. Of the 154 patients under therapy, 137 responded favorably with hematologic remissions lasting to forty-eight months. (Table III.) Bierman [28] noted six-month remissions in 50 per cent of his cases.

TEM. Triethylene melamine has proved effective in thirty-six of sixty-four cases of chronic granulocytic leukemia. Table IV records a poor response in three cases of acute leukemia. The length of remissions in the chronic form is shorter than that noted with myleran.

ACTH and Cortisone. These hormones are useful in the management of acute granulocytic leukemia. (Table V.) The number of cases (thirty-five) and the number of remissions (fifteen), however, are not as impressive as the results with myleran or TEM on chronic granulocytic leukemia.

Miscellaneous Agents. Table II presents the results of treating 396 patients with ten chemotherapeutic agents. The total of 116 responses is not striking, but a number of reports fail to record the number of patients showing improvement. However, 6-MP and aminopterin were more effective in the acute type of leukemia, while Fowler's arsenic solution and urethan produced a number of good remissions in chronic granulocytic leukemia.

TABLE I
CHEMOTHERAPEUTIC MANAGEMENT OF GRANULOCYTIC LEUKEMIA

Agent	Total No. of Cases	Acute Cases (No.)	Chronic Cases (No.)	Improvement (No. of Cases)
Myleran®	154	..	154	137
TEM	64	3	61	36
ACTH, cortisone	35	28	...	15
Miscellaneous	396	36	360	116
Totals	649	67	575	304

Review articles and material on technics or theory are not included in this survey of the literature since 1949.

Acknowledgment: The National Library of Medicine and the libraries of Furman University and the Greenville General Hospital made available the original literature for this study.

TABLE II

MANAGEMENT OF GRANULOCYTIC LEUKEMIA WITH MISCELLANEOUS AGENTS

Total No. of Cases	Acute Cases (No.)	Chronic Cases (No.)	Remissions (No.)	Comments on Therapy (Ref. No.)
140	..	140	..	P^{32}; statistically significant prolongation of life [27]
61	..	61	..	P^{32}; statistically significant prolongation of life [26]
20	..	20	13	P^{32}; all patients had leukocytic count under 30,000 per cu. mm. for 6 to 35 mo. [25]
14	..	14	..	P^{32}; less isotope needed for response in women [7]
19	..	19	18	Fowler's solution; good clinical, hematologic response [36]
19	..	19	18	Fowler's solution; remission to 30 mo. [24]
17	..	17	..	Urethan; some brief remission [34]
11	..	11	4	Urethan; one complete, three partial remissions [24]
11	..	11	1	Urethan; one satisfactory remission [36]
8	..	8	8	Urethan; rectal suppositories gave excellent results [41]
15	15	...	15	6-MP; good remission in terminal cases [8]
5	5	...	..	6-MP; some remission [16]
1	..	1	..	6-MP; no effect [32]
7	3	4	7	Dimethylmyleran (CB2348); prompt clinical, hematologic remission [6]
12	..	12	12	Demecolcine; number of granulocytes returned to normal in blood and almost normal in bone marrow [13]
6	..	6	..	Demecolcine; good remission [14]
3	3	...	..	Aminopterin; no response [39]
10	10	...	7	Aminopterin; complete remission [44]
6	..	6	3	Radiogold; clinical improvement [1]
1	..	1	1	Splenectomy; good remission [18]
9	..	9	9	Thio-TEPA; some clinical and/or hematologic remission [45]
1	..	1	..	Thio-TEPA; crystals of uric acid caused obstruction [23]

TABLE III

MANAGEMENT OF GRANULOCYTIC LEUKEMIA WITH MYLERAN

Total No. of Cases	Acute Cases (No.)	Chronic Cases (No.)	Remissions (No.)	Comments on Therapy (Ref. No.)
32	..	32	32	Brief but complete hematologic remission [21]
22	..	22	22	Hematologic remission and subjective improvement for 1 wk. to 12 mo. [22]
21	..	21	17	Significant remissions to 48 mo. [19]
19	..	19	14	Clinical and hematologic remission of 1 to 31 mo. [37]
15	..	15	15	Long remission and good toleration [5]
12	..	12	12	Clinical and hematological response; four of six patients who died had terminal acute leukemia [12]
12	..	12	7	Good clinical, hematologic remission to 13 mo. [10]
11	..	11	8	Subjective and objective improvement [31]
10	..	10	10	Subjective and objective improvement; four patients symptom-free [15]

TABLE IV

MANAGEMENT OF GRANULOCYTIC LEUKEMIA WITH TEM

Total No. of Cases	Acute Cases (No.)	Chronic Cases (No.)	Remissions (No.)	Comments on Therapy (Ref. No.)
16	..	16	5	Good clinical remission [20]
9	1	8	6	Three complete clinical, hematologic remissions of 35 to 107 days in chronic cases and three partial remissions; poor response in acute cases [40]
8	..	8	8	Best response of all neoplasms treated [2]
8	..	8	7	Five remissions of 3 to 10 wk.; two remissions for 6 to 7 mo. [3]
8	2	6	2	One good, one fair remission in chronic cases; no effect on acute cases [43]
6	..	6	5	Four good remissions, one fair [4]
4	..	4	1	Good remission [24]
4	..	4	1	Good response [36]
1	..	1	1	Good remission [35]

TABLE V

MANAGEMENT OF GRANULOCYTIC LEUKEMIA WITH ACTH AND CORTISONE

Total No. of Cases	Acute Cases (No.)	Chronic Cases (No.)	Remissions (No.)	Comments on Therapy (Ref. No.)
9	9	..	6	ACTH, cortisone; good clinical, hematologic remissions of 3 wk. to 2 mo. [30]
8	8	..	4	Prednisone, prednisolone; one complete, three partial remissions [17]
7	..	..	4	ACTH; complete remission of agranulocytosis [42]
5	5	..	1	ACTH, cortisone; slight remission but condition of two patients made worse [33]
3	3	..	..	ACTH, cortisone; no effect on acute and subacute cases [38]
3	3	..	..	ACTH, cortisone; complete but brief remission in 50 per cent of cases [9]
..	..	..	..	ACTH, cortisone; brief remission in thirteen of thirty cases of acute granulocytic and lymphocytic leukemia [11]
..	..	..	..	ACTH, cortisone; best remission in acute granulocytic and lymphocytic leukemia [29]

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Sciatic Hernia

A CASE OF CONGENITAL OCCURRENCE

LEO B. GAFFNEY, M.D., *Washington, D. C.*, AND JOSEPH F. SCHANNO, M.D., *Silver Spring, Maryland*

SCIATIC herniations are the rarest types of hernias encountered in a surgical practice. They represent a protrusion of abdominal viscera through the greater or lesser sciatic foramens. The incidence is equal in both sexes and may be found in persons of any age.

The hernia may be congenital or acquired following injury or surgery in this area. Sciatic hernias may present no visible signs, and only become evident after small bowel obstruction has occurred within the sac. However, they usually present themselves as a mass in the gluteal region, which may or may not be reduced. There may also be an impulse on straining. Due to the anatomy about the sciatic notch, the hernia always follows the path of the sciatic nerve as it enlarges. Sciatic pain may be the first clue as to the presence of the hernia.

Up to 1948, Watson [1] had collected thirty-five cases of sciatic hernias. Four of these were in children under one year of age. We were able to collect three additional reports published since then. All of these cases were of the suprapyramidal variety, two in males and one in a female. One patient presented with signs of bowel obstruction [2], the second with a mass in the gluteal area [3], and the third, a woman, showed signs of repeated urinary infection [4]. In this last case x-ray studies revealed a herniation of the ureter through the sciatic notch.

The anatomy of the gluteal area is complex, and the major points are of surgical importance. The sciatic notch is divided into the greater and lesser sciatic foramens by the sacrotuberous and sacrospinous ligaments. The greater foramen is further divided into a suprapyriformic and infrapyriformic portion by the pyriformis muscle. The superior gluteal nerve and artery, which is the first branch of the internal illiac artery, exits through the superior portion. Care must be taken not to injure this vessel as it may retract into the pelvis and continue to hemorrhage.

The sciatic nerve is most instances exits below the pyriformis muscle, although in rare cases, portions of it may traverse the muscle. The gluteus maximus muscle overlies this area, and its fibers must be separated in the surgical approach.

It can be seen that it is possible to have the hernia in three distinct locations: suprapyriformic, infrapyriformic and, lastly, subspinous, coming through the lesser sciatic foramen. The subspinous variety lies deep to the obturator internus muscle. Only one such case has been reported [1]. The internal opening of the hernia is in the posterolateral aspect of the pelvis. In the female it is easily located at the base of the posterior aspect of the broad ligament.

Two approaches are possible for surgical correction. If the diagnosis is certain, transabdominal attack through a midline laparotomy is the safest. The sac and contents are everted. The sac is excised and bowel resection performed if necessary. It has been suggested that the defect in the sciatic notch be closed by fascial transplants, tantalum mesh or sliding a patch of pyriformis fascia.

When the diagnosis is in doubt, the gluteal approach will usually be used. An oblique incision is made from the posterosuperior spine down over the greater trochanter. The sac will usually be located beneath the gluteus maximus; these fibers must be separated. All bowel resections should be performed through an abdominal incision regardless of the primary approach. The reader is referred to the books "Hernia" by L. F. Watson [1] and "Surgery of the Alimentary Tract" by Shackelford [5] for illustrations of the surgical anatomy of sciatic hernia.

CASE REPORT

A five month old white female child was admitted to the surgical service with a chief complaint by the mother of a "mass in the left buttock since birth." The patient was born at another hospital at which time the mass was noted. Gestation, delivery, growth and development to the present age were normal. The mother stated that the mass was rather firm, non-tender and had enlarged proportionately with body growth. Bowel, urinary and neuromuscular function of the extremities were normal for her age. Physical examination was negative except for a soft bulging mass over the left gluteal area measuring 2 by 3 cm. The mass was not reducible. Laboratory studies were normal. Differential diagnosis included teratoma, lipoma, chordoma and hernia.

Surgical approach was through the gluteal area. The sac actually pierced through the fibers of the gluteus maximus muscle and was located in the subcutaneous tissues. Upon retracting the fibers, the hernia was identified as such, of the suprapyriformic variety.

The sac was opened and found to be empty. Branches of the superior gluteal artery were distributed over the sac wall. The sac was ligated at the base and excised. There was some mild oozing from the superior gluteal artery, and the defect was packed with gelfoam. The pyriformis muscle was sutured to the superior edge of the gluteus maximus fibers, along with the gluteus medius. At no time was the sciatic nerve seen. The patient's postoperative course was uneventful and one year following surgery there is no evidence of recurrence or disability.

SUMMARY

The incidence, anatomy and surgical correction of sciatic hernias is reviewed, and a case of sciatic hernia, present from birth, is presented.

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The Use of a Quilting Stitch for the Repair of Indirect Inguinal Hernia

RENÉ ARCHAMBAULT, M.D., H. A. ARCHAMBAULT, M.D., *Wayne, Michigan,* AND
N. J. MIZERES, PH.D., *Detroit, Michigan*

EVER since the time of Halsted [3] and Bassini [1], numerous modifications of hernial repair have been devised. A new modification of the original Halsted repair has been devised which seals off the inguinal canal in those direct hernias where there is marked atrophy of the tissues; it appears to be stronger than either the Bassini or Halsted repair. The method will be described and the technic applied for testing its strength.

The recurrence rate is one of the clinical criteria used in evaluating repairs. According to Clear [2] a ten-year period of follow-up is required. This type of study is feasible when dealing with a select group of patients, such as veterans, since they usually return to a government institution more readily than do patients from the general population. As a result it becomes difficult to evaluate recurrence rates of follow-ups in non-government hospitals. Because of this difficulty it was decided to test the new type of repair in the laboratory using cadaver material. Although long clinical experience must be the ultimate test for any procedure, laboratory testing has the advantages that one can use as controls successive repairs on the same or opposite sides of the same cadaver. Furthermore, a cadaver is not subject to the extremely variable factors of activity, diet, emotional stress, disease, etc. Of course, such experiments are designed to test only the strength of the repair and cannot be compared to the living individual in regards to intra-abdominal pressure, elasticity, or strength of tissues.

The new repair is essentially a modification of the Halsted technic. A quilting type stitch (Fig. 1) is placed in the medial edge of the internal ring and three additional stitches in the rest of the inguinal canal. This type of suturing approximates all the layers of the wall of the inguinal canal, including the peritoneum, thus providing a strong resistance against a recurrent indirect hernia. It is suitable in cases in which debility, senility, long-standing use of a truss or an extremely large hernia present a weak conjoined tendon and thinned out abdominal muscles in the wall of the inguinal canal. For such cases this repair has been used for a number of years in the Nankin Clinic with excellent results. Where the muscles of the abdominal wall are normal, however, the Halsted repair is used.

The inguinal canals of ten cadavers, nine males and one female, ranging from forty to seventy years of age, were used in the experiment. The apparatus (Fig. 2) consisted of a single pulley and a strong malleable copper wire, one end of which was threaded through the inguinal canal and internal ring. A transverse incision was then made through the abdominal wall just inferior to the umbilicus. This permitted visualization of the internal ring and the end of the copper wire to which a stainless steel, bullet-shaped cone was attached. (Fig. 2.) At the other end of the copper wire weights were attached until the cone was pulled through the inguinal canal and the external inguinal ring. In this way an artificial indirect hernia resulted. Surprisingly enough, avulsion

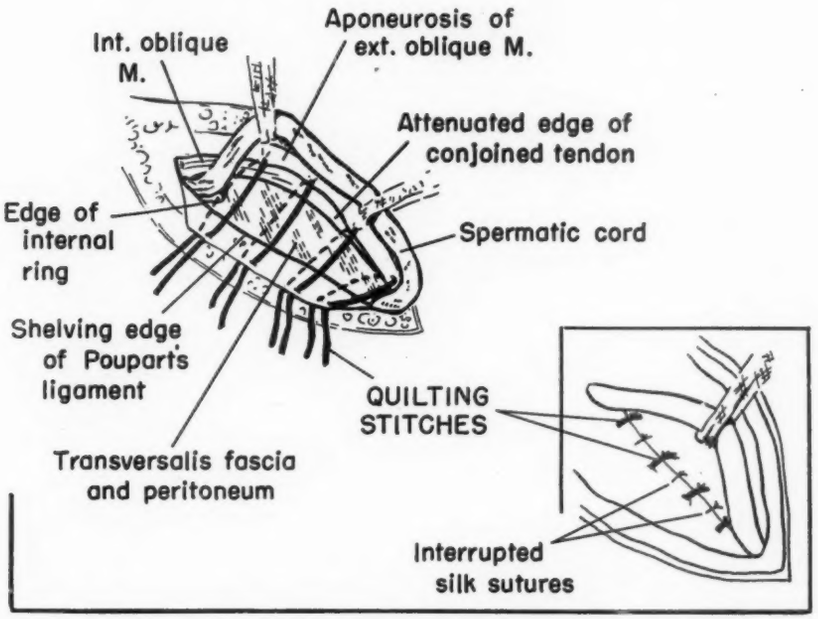

FIG. 1. Drawing of the new repair using a quilting-type stitch. Note that one of the four stitches includes the medial edge of the internal inguinal ring. The wall is closed by approximating all the layers, including the peritoneum, and the cord is transplanted external to the external oblique aponeurosis. Sketch shows that the vertical sutures accomplish the following: (1) they buttress the weakened transversalis fascia and peritoneum with the strong aponeurosis of the external oblique muscle, and (2) they close off the inguinal canal.

FIG. 2. Photograph of the apparatus used in testing the strength of the new repair.

of the walls of the canal was negligible. It required from 6 to 14 kg. to pull the cone through the normal canal. The canal, thus herniated, was then repaired by the Bassini technic. The opposite canal was then herniated in the same manner and this time the Halsted technic was used. After five trials it became apparent that the cone required from 10 to 22 kg. for it to emerge through the external ring after the Halsted repair while after the Bassini it required from 5 to 13 kg. weights. (Table 1.) The Halsted repair was then compared with the new technic. After five trials it was apparent that it took from 14 to 28 kg. for the cone to emerge through the external ring after this new repair. (Table 1.) In two cases the weights raised the body above the table before the cone finally emerged through the external ring.

TABLE 1
COMPARISON OF BOTH BASSINI AND HALSTED WITH THE NEW REPAIR

Bassini and Halsted I Repairs

	Normal	Bassini	Halsted I	Ratios
Cadaver No. 1, male:				
Right	10 kg.	5 kg.	.....	0.5 B†
Left	9 kg.	.....	12 kg.	1.3 H‡
Cadaver No. 2, male:				
Right	11 kg.	13 kg.	.....	1.1 B
Left	8 kg.	.....	15 kg.	1.9 H
Cadaver No. 3, male:				
Right	15 kg.	.....	20 kg.	1.3 H
Left	13 kg.	13 kg.	.....	1.0 B
Cadaver No. 4, male:				
Right	8 kg.	.....	10 kg.	1.3 H
Left	7 kg.	7 kg.	.....	1.0 B
Cadaver No. 5, male:				
Right	6 kg.	8 kg.	.....	1.3 B
Left	10 kg.	.....	17 kg.	1.7 H

Halsted I and New Repair

	Normal	Halsted I	New Repair	Ratios
Cadaver No. 6, female:				
Right	7 kg.	.....	15 kg.	2.1 NR§
Left	13 kg.	22 kg.	.....	1.7 H‡
Cadaver No. 7, male:				
Right	15 kg.	20 kg.	.....	1.3 H
Left	6 kg.	.....	10 kg.	1.7 NR
Cadaver No. 8, male:*				
Right	15 kg.	.....	28+ kg.	1.9 NR
Left	13 kg.	18 kg.	.....	1.4 H
Cadaver No. 9, male:*				
Right	11 kg.	14 kg.	.....	1.3 H
Left	14 kg.	.....	27+ kg.	1.9 NR
Cadaver No. 10, male:				
Right	9 kg.	.....	14 kg.	1.6 NR
Left	10 kg.	10 kg.	.....	1.0 H

* In cadavers Nos. 8 and 9 the steel cone did not go through the external inguinal ring.
† Bassini.
‡ Halstead.
§ New repair.

The factors affecting this type of experiment must be analyzed before coming to any conclusions. The direction of pull, in the case of the Bassini repair, was made parallel with the position of the inguinal canal since a hernia after this type of repair presents itself in the same oblique plane as the canal. In the Halsted and new technic the direction of pull was made at a lateral angle of approximately 100 to 130 degrees. Since the new opening in the external oblique aponeurosis for the cord is made to correspond with the level of the internal ring the protrusion of a recurrent hernia is not in line with the plane of the inguinal canal. The most important variable factors are the type of silk and the surgical repair. A heavier gauge silk increases the strength of the repair. It was therefore important to standardize the gauge of silk for all the repairs. The one used in these experiments was a black braided surgical silk, gauge 3-0. For the new repair, in the first two experiments, only one quilting stitch was used at the internal ring. Later it was determined that the repair was strengthened when four quilting stitches were used throughout the wall of the canal.

SUMMARY AND CONCLUSIONS

Ten cadavers were used to determine the strength of a new repair in indirect inguinal hernia. A copper wire was threaded through the inguinal canal by entering the internal inguinal ring. A steel cone was attached to the wire while in the peritoneal cavity. The other end of the copper wire passed through a simple pulley and weights were attached to this end of the copper wire, exerting a pulling force on the steel cone. By adding sufficient weight an artificial indirect hernia was produced in the normal canal. Using the Halsted and Bassini repairs and comparing them with the new repair it was concluded that the Halsted and the new repair offered greater resistance than the Bassini. It was also observed that this new method of stitching reinforces the walls of the inguinal canal to such an extent as to offer on the average a greater resistance to the pulling force of the steel cone than the Halsted repair.

When the tissues are in good condition the new repair offers no advantage over the

Halsted. But in cases in which the transversalis fascia and conjoined tendon are weak it buttresses the peritoneum and transversalis fascia with the strong external oblique aponeurosis, thus offering a decided advantage. In regard to the new repair the following points must be emphasized: (1) Since the method involves a quilting-type stitch it is imperative that the cord must be transplanted external to the aponeurosis of the external oblique to prevent strangulation. (2) It is advocated that the first quilting stitch should be made to include the medial edge of the internal inguinal ring. (3) It is of value to close the inguinal canal with the addition of three more quilting stitches.

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A Simple Tray for Emergency Hand Surgery*

KENT L. BROWN, M.D., *Cleveland, Ohio*

INJURIES to the hand have become one of the most frequent emergencies seen in hospitals today. Many of these injuries are bleeding, contaminated wounds which require meticulous débridement with extensive cleansing and irrigation before repair.

It has been the practice, in most surgeries to support the hand and arm on an arm board or side table covered with sterile drapes and let the cleansing agents, greasy contaminants, irrigating fluid, and portions of tissue fall where they may. This is messy for the operating room and the surgeon.

The commonly used emergency room attachable metal armrest lacks stability. The wooden armrest, which passes beneath the mattress of the table, or cart, and is held by the patient's weight, is also unstable. The usual side table, with casters removed, is stable, but often awkward in size and its legs compete for space with the legs of the surgical team. In 1953 Davis et al. [1] designed a tray which overcomes some of these objections.

I propose a firmly attachable basin-type tray, suitable for emergency or definitive surgery of the hand. This tray is constructed in two parts. (Figs. 1, 2 and 3.) It lends neatness to the operative procedure, cuts down cleaning of the operating room between cases, and provides an adequate working surface with a readily available irrigating nozzle. It is handled easily by the nursing staff, has a minimal number of components, is light, and can be autoclaved with relative ease.

For the standard operating table the clamp portion fits tightly by means of either of two attachments. One is held by a single wing nut (Fig. 4) while the other fastens by a catch lock. (Fig. 5.) An attachment is also made for a wheeled operating cart or stretcher cart. (Fig. 6.) The clamp does not require sterilization. The operating portion of the combination is a stainless steel pan, 2 inches deep.

A tongue from the edge of the pan has a slide arrangement which attaches to the clamp. It is easily slid into position, without contamination, and is adjustable to arm length. It is tightly secured by a single knurled nut.

The pan part, which is kept sterile, has a drain in its outer edge to which a rubber tube is attached. This tube directs the debris and fluids into a drainage bucket. The surface of the pan is covered by a coarse stainless steel mesh which lends stable support for the hand and allows fluid and particles to pass readily into the pan, and then to the bucket. After cleansing and débriding, a small sterile pad or drape may be placed over the pan if desired.

In the outer edge of the meshed operating surface, and attached to it, directly over the drain hole, is a metal tube for holding the irrigating nozzle when not in use. Because this tubular holder is over the drain outlet, it is possible to insert the irrigating nozzle into the outlet and force through any materials which may be plugging it. This holding tube is also constructed so that it acts as a handle to remove the mesh from the tray for cleaning.

A single supporting leg may be attached to the tray by a wing nut. This is used when conventional operating tables or emergency room operating wheeled carts lack stability. This tubular support fits into a metal sleeve which is a part of the tray and which allows adjustment for table height.

In 1950 I designed a stainless steel hand operating tray which was suitable for irrigation, but did not attach to the operating table. The drain hole was on the end nearest the operating table. It was designed so that it tilted to allow flow toward the drain outlet. The irrigating nozzle was held in a support which was retract-

* This investigation was supported by Pemco Inc., Brecksville, Ohio, from whom the tray is available.

Tray for Hand Surgery

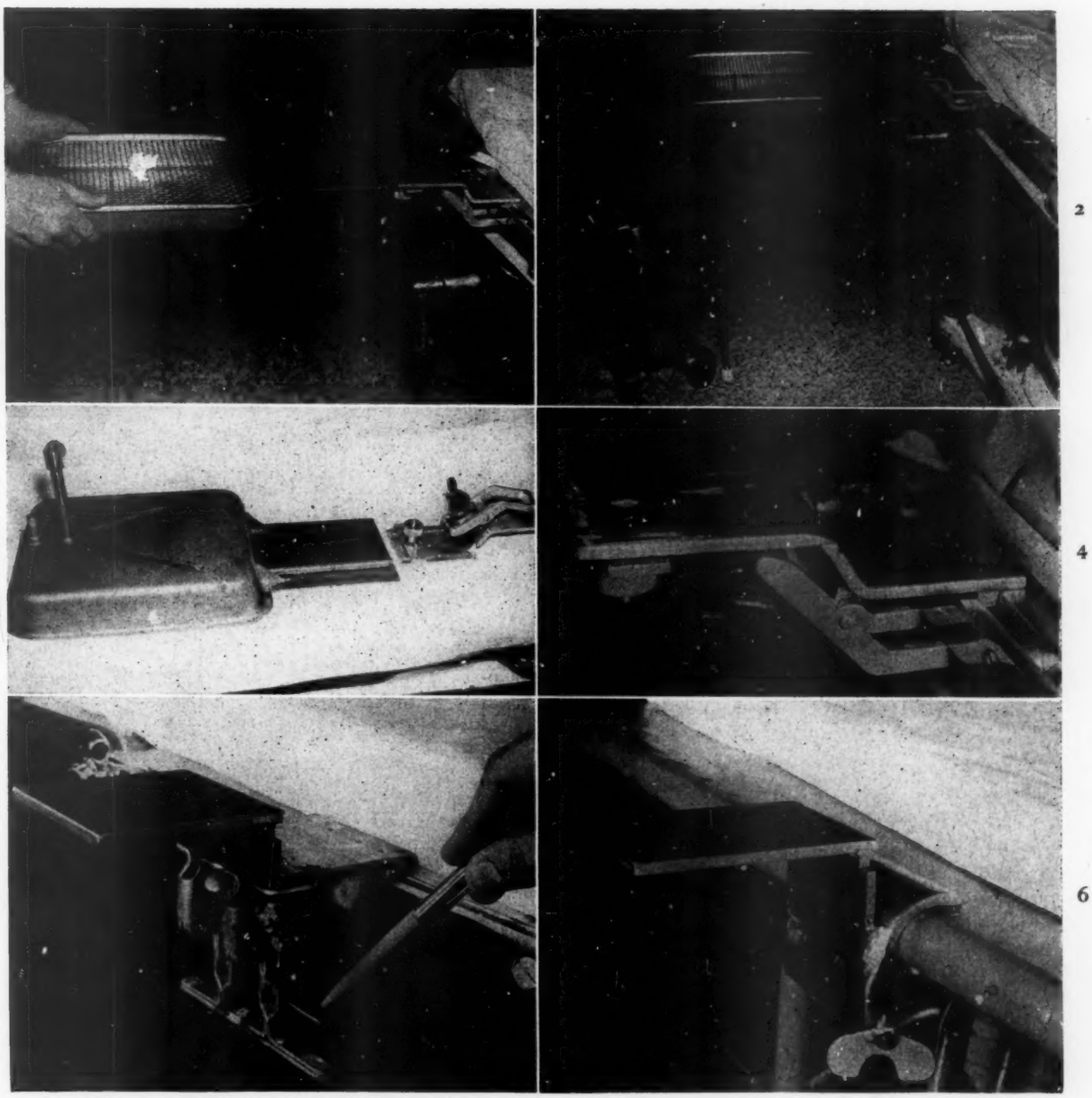

FIG. 1. Clamp attached to standard operating table by single wing nut. Tongue of tray can be slid into position for attachment.

FIG. 2. Clamp and tray attached. Irrigating nozzle in place. Drainage tube attached. Leg support adjusted for working height.

FIG. 3. Bottom of pan showing rib supports and slide attachment to clamp.

FIG. 4. Clamp for standard operating table. Attached by single wing nut.

FIG. 5. Catch lock clamp for standard operating table. Depression of part illustrated releases clamp.

FIG. 6. Stable clamp for wheeled, operating or stretcher carts. Curved portion fits over rubber bumper.

FIG. 7. Tray in use.

able for convenience in wrapping and autoclaving the unit. The pan, which was covered with a removable heavy stainless steel mesh, measured 18 inches by 20 inches and was 2 inches deep. It was heavy, difficult for nurses to handle, and required a four-leg table for support.

The tray now suggested measures 11 inches by 13 inches and is 2 inches deep. It weighs under 4 pounds, is easily cleansed, autoclaved and stored. It serves the purpose of other irrigating trays without the bulk. It is convenient for emergency room use where space is limited. It also lends itself to definitive hand surgery. (Fig. 7.)

SUMMARY

A simple, stable, practical hand irrigating tray is presented which should increase efficiency in operating rooms for the care of the wounded hand. It is constructed for the convenience of the surgeon and nurses. It decreases labor for cleaning between cases and cuts down delay.

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New Uses for an Old Instrument

COL. S. W. FRENCH, III, M.C., *San Francisco, California*

From the Thoracic and Cardiovascular Surgery Service, Department of Surgery, Letterman Army Hospital, San Francisco, California.

THE illustrations show curved and straight Doyen intestinal clamps covered with white shoestrings. (Fig. 1.) I have used this modification of the Doyan clamp for several years and have found it to be a very useful and versatile instrument.

FIG. 1. Curved and straight Doyen clamps with and without shoestring covers.

With the cloth covers there is absolutely no slipping of the clamp. There is no tissue injury because these are non-crushing clamps.

We have found this clamp to be very useful in gastric and small and large bowel surgery. (Figs. 2, 3 and 4.) After excision of the diseased area of stomach or bowel, the clamps are released and all bleeding points secured following which the clamps are reapplied and the anastomosis carried out.

Wedge resection of the lung is easily performed with these instruments; as a result no crushed lung tissue is left in the thoracic cavity after completion of the operation (Fig. 5.) The curved clamp adapts itself admirably to application across the cardiac end of the stomach when suturing bleeding esophageal

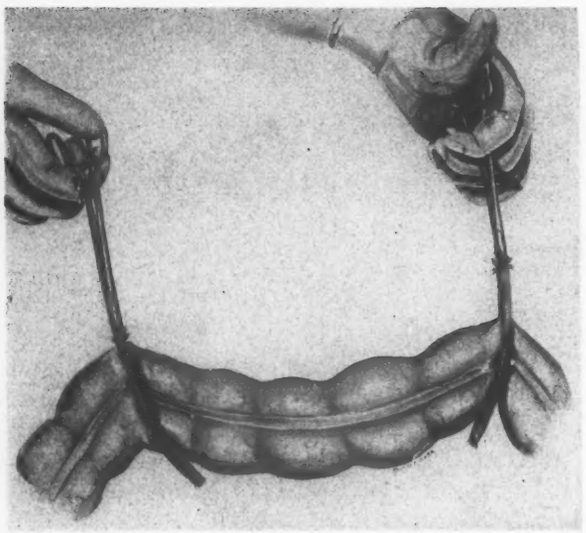

FIG. 2. Use of clamps in performing resection of the large bowel.

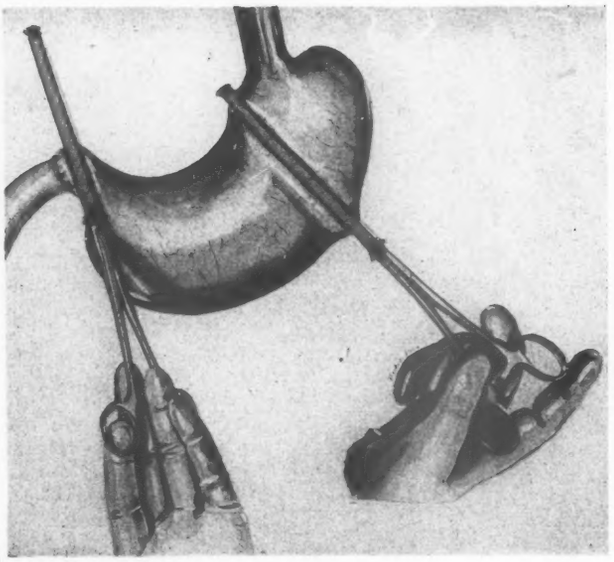

FIG. 3. These clamps provide adequate hemostasis in gastric surgery.

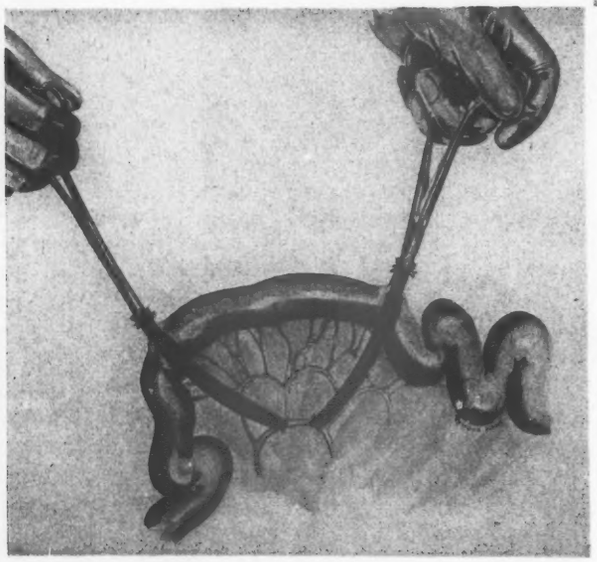

FIG. 4. Use of clamps in performing resection of the small bowel.

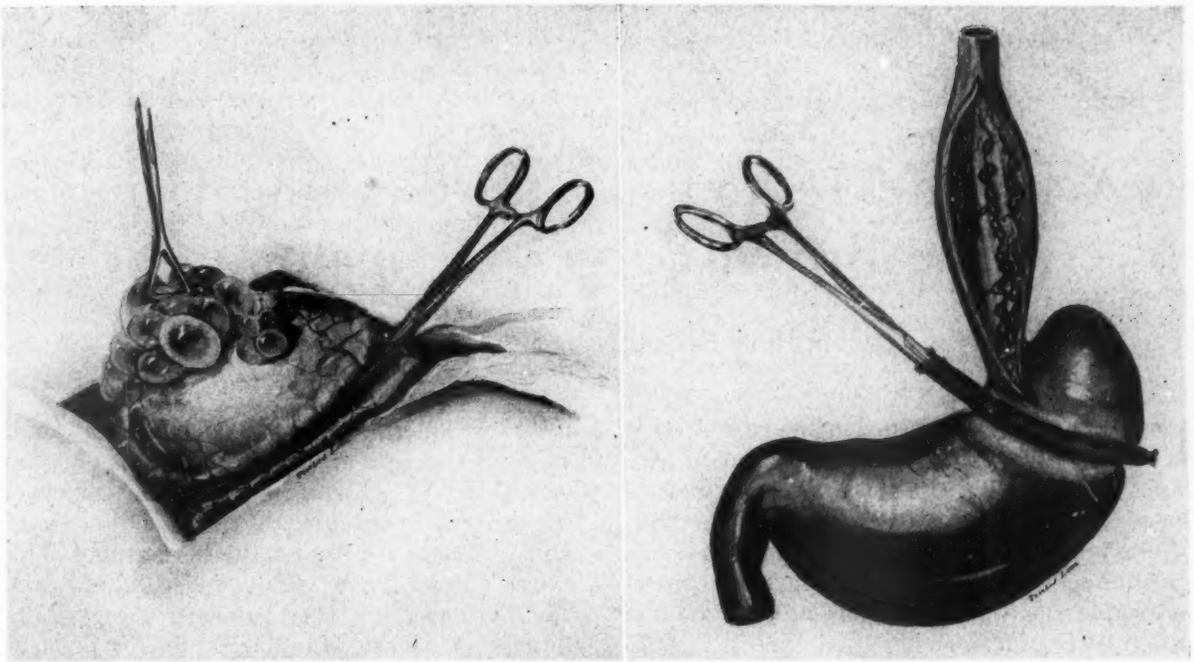

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FIG. 5. Application of clamp when performing wedge resection of the lung.

FIG. 6. Application of clamp across cardiac end of stomach when performing transthoracic ligation of bleeding esophageal varices.

varices. (Fig. 6.) This operation is usually accompanied by much uncontrollable hemorrhage, but with the clamp surgery is usually bloodless and the varices can leisurely be completely ligated. Obviously this decreases the need for multiple blood transfusions in these patients.

As a kidney pedicle clamp there is no danger of crushing the vessels with the difficult and severe hemorrhage which usually ensues.

These clamps can also be used on large blood vessels, as for example the aorta and venae cavae.

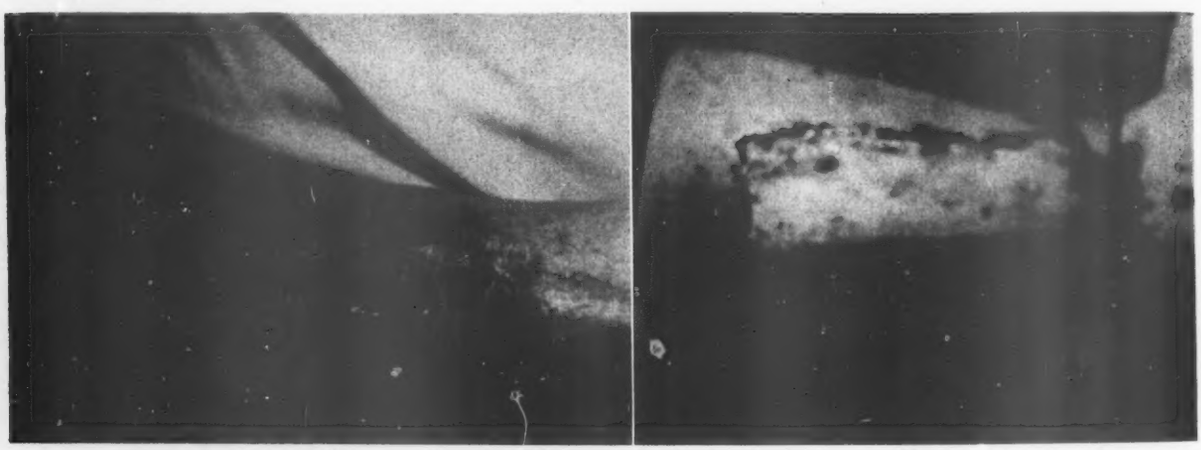
A Rapid Method of Skin Grafting Using the Brown-Berger Dermatome

CALVIN REED BROWN, M.D., *Salt Lake City, Utah*

IN this day of threatened mass casualties it is imperative that we be prepared to give rapid definitive treatment to large numbers of severely burned patients. Our present methods of plastic surgery are so cumbersome and time consuming that their use in large numbers of burn cases such as result from an atomic blast would be impractical.

A comparatively recent innovation in the field of skin grafting has been the Brown-Berger dermatome. This electric clipper-like apparatus has been widely tried and rejected by many because of its purported variation in thickness of cut and inaccuracy. Its ease in handling and rapidity of action, however, make it an ideal instrument for the mass skin grafting technics which might be necessary in atomic disasters.

Method. After the wound has had opportunity to granulate, its dimensions are surveyed and the location of the donor site is selected. The width of cut is then adjusted to ¼ inch beyond the edges of the wound. A thin layer of mineral oil is placed over the donor site and a section of split-thickness skin of that width and ¼ inch longer than the length of the wound is obtained by placing downward and forward pressure on the dermatome. This skin is spread out on sterile, moist saline gauze. The dermatome is then run over the granulation tissue of the wound in a similar fashion. This procedure removes the excess granulations and prepares a smooth, clean bed for the donor skin of precisely the same dimensions. The skin is then gently laid over the defect after oozing of the recipient site has diminished. A strip of telfa dressing slightly larger than the wound makes suturing unnecessary although anchor sutures help to prevent slippage. Actually the absence of sutures helps to prevent infection and foreign body reaction so common in skin grafting. The entire wound is then covered by a pressure dressing with ace bandages or elastoplast, being cautious not to slide off the donor skin in the process. (Fig. 1.)



1A 1B

FIG. 1. A, lesion of leg prior to treatment. B, lesion after débridement with dermatome and application of graft as described.

The entire procedure can be accomplished in a matter of minutes; and if enough dermatomes are available for rapid sterilization, the only delay will be in anesthesia. Afrer ten days to two weeks most grafts will be found to show 100 per cent healing with minimal infection and foreign body reaction. A neat, rectangular recipient site with little scarring should result.

SUMMARY

The method proposed for rapid skin grafting of mass casualties need not be limited to large numbers but is most ideally suited for this type of work. It has been used extensively by the author in individual cases and found to yield the best results of any rapid method of skin grafting tried.

Cholecystectomy Technic

SIDNEY VERNON, M.D., *Willimantic, Connecticut*

GALLBLADDER surgery is generally regarded as difficult. A departure from traditional technic might increase the facility of the procedure. For cholecystectomy the surgeon usually stands on the right side of the patient; from this side he has a tangential view of the under surface of the liver. To put his right index finger in the foramen of Winslow, the surgeon must first lay down the instrument he holds; to use his left hand he must twist his shoulder and elbow muscles to a cramped position. The assistant standing on the left side can see better and the surgeon must be able to count on the assistant's skill.

If the surgeon himself stands on the left side, his view of the operative area is improved. It is not obstructed by the wound edge or subcostal margin and visualization of the operative area requires a minimum of retraction. The left hand with which he reaches down to place a finger into the foramen of Winslow reaches with ease and maintains the position without strain. The surgeon's use of his left hand to assist in the dissection of the cystic artery and bile ducts may then be continuous throughout the operation. The difference in morbidity between a simple cholecystectomy and one with choledochostomy added demands judgment that will lead the surgeon to do what is necessary, no more, no less. Statistics do not help, for one surgeon opens the common duct in 48 per cent of his cholecystectomies, another in 10 per cent. Higher percentages may be more justified in more experienced hands, but the extent of the surgery should be determined by the patients' needs, ascertained by careful observation. Ogilvie advises not opening the duct if it is narrow, aspirates clear yellow bile and no irregularity is felt from hilum to papilla. Palpation during dissection offers a guide as to whether the common duct should be opened or left alone.

If in the course of the procedure, bleeding arises, there is no temptation for rash action with a clamp; simple thumb and finger compression of the hepatic artery is instantly possible while suction, revisualization and clamping of only the cystic artery is accomplished.

When concepts of pathology and anatomy appear to be in conflict, the surgeon must determine what to do from his findings. Womack urges that the common duct be stripped of nerves in order to avoid neuromas. Appleby (Canada) contends that the blood supply to the common duct may come from nearby arteries through a row of short arterioles. Thus, stripping of the common duct would deprive it of blood supply to produce necrosis, fibrosis and stricture of the duct. Also, sight and touch are both needed to guard against the too frequent variant right hepatic artery which can be mistaken for a cystic artery. Recurring inflammation may in effect further shorten a short cystic artery into a sigmoid form adherent to the gallbladder. The duet of sense impressions aids avoiding the error of cutting the right hepatic artery. In tying the cystic duct, too much zeal for leaving no stump should not result in tenting of the common duct with placement of a tie that narrows its lumen. The ulnar side of the surgeon's hand supplements retraction of the bowels away from the under surface of the liver by the second assistant. For retraction in the upper abdomen the added aid is appropriate because of the effect of diaphragmatic motion.

On the question of blunt or sharp dissection, some would insist on nothing but sharp dissection of the cystic artery and duct. Accurate, non-bloody dissection as an objective is better than adherence to a rigid rule of technic. Sharp dissection must be used for the peritoneal covering, and parallel strokes made along the course of the cystic duct and artery with a gauze peanut (Küttner) seem more rational and safe. Blunt dissection through fat areas to

delineate the fat from the discrete structures has long been standard surgical technic.

The incision for cholecystectomy should depend on the total events during and after the surgery. For the difficult case many surgeons prefer infracostal incision. For safety against postoperative dehiscence Gurd has popularized the horizontal incision. The vertical incision, which transects the fewest abdominal wall structures, may seem logical for the resident surgeon and it lends itself for working high and low in the abdomen; yet the greater postoperative discomfort of the vertical incision is sufficient reason to avoid its routine use. If preoperative study clearly shows that the surgery will be confined to the biliary tract, the infracostal seems the best incision. Advantages gained for the difficult case by this incision should be retained for the easy case.

Standardization has advanced surgical science, yet standards should not be rigid ceremonials; they can be thoughtfully reexamined to advance the art of surgery. The dexterity characteristic of the surgeon's hands is associated with the agility of his mind as well.

Thrombosis of the Terminal Aorta and Horseshoe Kidney

DAVID S. HUBBELL, M.D., *St. Petersburg, Florida*

THROMBOSIS of the distal aorta and iliac arteries, described by Leriche [*1,2*] and others, is characterized by symptoms of claudication of hips and lower extremities, impotence, and diminished or absent arterial pulses beyond the aortic bifurcation. Within the past fifteen years it has been increasingly recognized as a clinical entity. More recently, methods of arteriography and surgery have greatly improved the efficacy of definitive diagnosis and treatment. The following case is of interest because of the presence of a horseshoe kidney, an unusual aortogram and serum lipid studies.

FIG. 1. Intravenous pyelogram showing the horseshoe kidney and silver clips following the first operation.

CASE REPORT

A forty-seven year old white married man was first seen on March 14, 1955 with the chief complaint of claudication of the hips and thighs. The past history and review of systems were within normal limits except as follows: In 1925 the patient suffered burns of both calf and popliteal areas and right side of the trunk. These healed with extensive painless scarring of those areas. Bilateral inguinal herniorrhaphies were performed in 1936. In 1943, while on long marches in the army, calf and thigh pains had developed. Approximately eighteen months before his first visit intermittent claudication of the calves developed; later it developed in the thighs and buttocks and gradually became worse. Three weeks before the patient's first visit progressive cutaneous ulceration developed in the scar areas on the right anterior shin and popliteal regions. He had not experienced a penile erection in more than one year.

Physical examination revealed a white man appearing older than his stated age. Blood pressure was 115/70 mm. Hg, pulse 80 and temperature 37.0°C. The only abnormalities were as follows: There was extensive pliable scarring of the skin of both legs and over the right side of the trunk, with an ulcer 4 by 5 cm. over the anterior tibial area and two smaller ulcers 2 by 2 cm. in the right popliteal region. These ulcers had flat, poorly granulating bases and flat, well demarcated, minimally hyperemic edges. There were no pulses in the iliac arteries nor in the arteries distal to them. Oscillometric readings were zero in the thighs and calves. There was no significant muscle or cutaneous atrophy. There was delayed venous filling and rapid blanching on elevation. Bilateral herni orrhaphy scars were present, as were some internal and external hemorrhoids.

Laboratory data during the period of observation revealed the following: Total and differential white blood cell counts, urinalysis, blood urea nitrogen, phenolsulfonphthalein secretion and fasting blood sugar determinations were all within normal limits. Serum cholesterol was 385 mg. per 100 ml.,

FIG. 2. Aortogram indicating complete block of left iliac artery and partial block of the right artery. This is false, since the aorta and iliacs were at that same time completely occluded. The dye has dissected between the thrombus and the vessel wall.

cholesterol esters were 365 mg. per 100 ml., or 88 per cent. The hemoglobin had been between 15.0, 13.3 and 16.0 gm. per 100 ml. of blood, and red blood cell count had been 5.35, 4.44 and 5.26 million per cu. mm. during the period of observation.

Plain films of the abdomen revealed a band of calcium 1.5 cm. wide at the bifurcation of the aorta.

It was believed that the patient had a thrombosis of at least the distal aorta and iliac vessels and laparotomy was undertaken, performing the aortogram on the operating table.

On April 4, 1955, a midline incision revealed thrombotic occlusion of internal, external and common iliac arteries and of the aorta, extending upward about 12 cm. The proximal edge of the thrombus lay beneath the joining bridge of a horseshoe kidney. (Fig. 1.) The inferior mesenteric artery was enlarged to six or seven times its normal size. The aortogram was performed by inserting a 17 gauge needle at the level of the third lumbar vertebra and injecting 16 ml. of 70 per cent urokon® into the lumen of the aorta. (Fig. 2.) An extensive thromboendarterectomy was performed. Longitudinal incisions were made into the aortic bifurcation and along either iliac artery, removing large amounts of organized thrombus (Fig. 3) with intima from the level of the kidney to the femoral arteries. The tunica media and adventitia were strong and intact. Bilateral lumbar sympathectomy was performed at that time. After operation there was active arterial pulsation at the level of the femoral artery on the right, but none on the left. The postoperative period was not remarkable.

The patient has been readmitted twice, once for skin graft to the right leg, and again for further sympathectomy on the right going up through the twelfth thoracic ganglion. Following the operation the legs were warmer and claudication in the thighs and buttocks gradually disappeared. He has been maintained on dicumarol,® a low fat diet and whiskey; he has also abstained from smoking. The only problem at present is in the old burned areas on the right leg, where there have been several non-malignant superficial ulcerations appearing and then gradually healing. When last seen twenty-eight months after operation, no pulses were

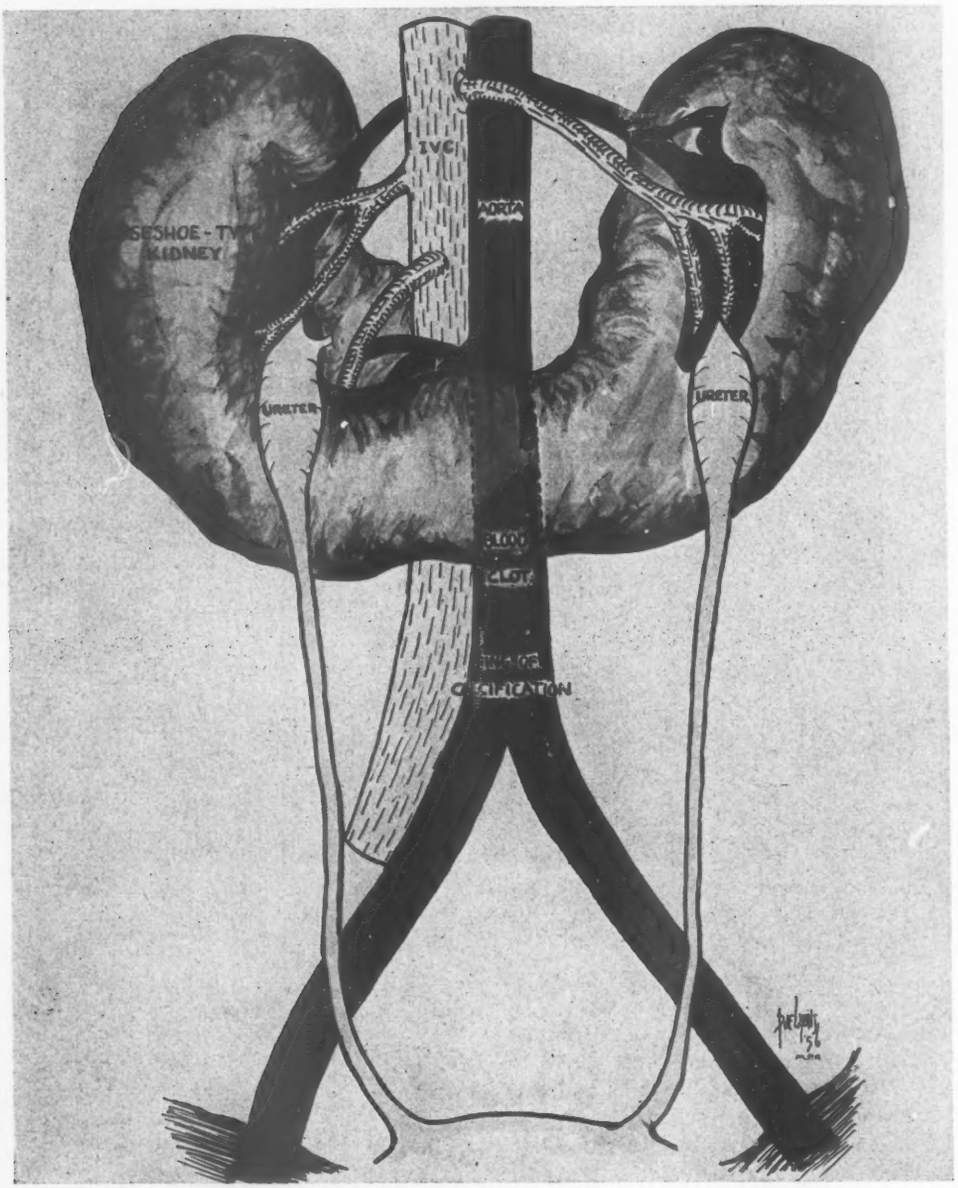


FIG. 3. Schematic representation of aortic thrombosis extending from beneath the renal isthmus down to the femoral arteries.

palpable below the inguinal ligaments. The patient works regularly as a salesman.

Since thromboendarterectomy serial determinations have been carried out on serum cholesterol, revealing a range of 350 to 455.5 mg. per 100 ml. The variations occurred while the patient was maintaining a well managed, low cholesterol, low fat diet. Serum lipoprotein tests, using the ultracentrifuge method of Gofman, revealed an atherogenic index of 151, with SF (Svedberg flotation) 0–12:638 mg. per cent, and SF 12–400:501 mg. per cent. After six weeks' therapy with monichol,® 5 ml. four times daily, the atherogenic index had increased to 183.

COMMENTS

The three most interesting features of this case are: (1) the presence of a horseshoe kidney with Leriche syndrome, (2) the false interpretation gained from the aortogram, and (3) the studies in lipid metabolism.

Presence of Horseshoe Kidney with Leriche Syndrome. In the available literature no other report has been found in which these two conditions coexist. The fact that the proximal level of the thrombus lay at the level of the aorta compressed by the renal tissue would

suggest that there was some compression or aggravation by the kidney. This also points out the desirability of carrying out a good aortogram before surgery, being certain to include the nephrogram phase in the films.

False Impression Gained from Aortogram. The operative aortogram revealed dye apparently filling the distal aorta, indicating a partial block in the right iliac and a complete block on the left. At the time the film was taken, however, these vessels were solidly filled by organized thrombus. This misleading pattern was due to a dissection of the dye between the thrombus and the arterial walls. The needle apparently had been inserted just distal to the proximal limit of the thrombus. Although some blood could be aspirated prior to injection of dye, there had been no free pulsatile backflow of blood into the syringe.

Studies in Lipid Metabolism. Theis [3], in discussing twenty-nine cases of thrombosis of the terminal aorta, found 75.0 per cent of those patients to have a cholesterolemia of over 300 mg. per cent, 24 per cent to be diabetic, and one patient with syphilis. Blood studies have shown that this patient has an abnormal lipid metabolism which was playing the major role in producing the arterial damage to the distal aorta. Although this patient does not have clinically demonstrable coronary artery disease, his lipoprotein patterns are similar to that group of relatively young persons who do have it. Lipid studies of this type are seldom reported in literature dealing with this disease.

SUMMARY

1. A case of a forty-seven year old man with Leriche's Syndrome and horseshoe kidney is presented. The upper limit of thrombosis within the aorta lay beneath the renal isthmus, which compressed the aorta.

2. A case of misleading findings on aortogram was shown, which was due to dissection of the dye between the thrombus and the arterial wall.

3. Blood lipid studies are presented.

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Carcinolytic Effect of Local Triethylenethiophosphoramide (Thio-TEPA) on Malignant Melanoma

HERBERT CONWAY, M.D., *New York, New York,* AND B. HEROLD GRIFFITH, M.D., *Chicago, Illinois*

From the Department of Surgery (Plastic), The New York Hospital-Cornell Medical Center, New York, New York.

THE effects of a great many chemotherapeutic agents on animal tumors and on human tumors transplanted to animals have been studied over the past few years. Some have proved to be of definite value and have prolonged the lives of patients with far advanced malignant tumors. So far, however, none of these compounds has been curative in man.

The beneficial effects of the chemotherapeutic agents are both subjective and objective. Among the subjective changes are euphoria, increased appetite, diminished pain and nausea, and improved morale. Objectively, decrease in ascites and hydrothorax, gain in weight, reduction of fever and decrease in size of tumors have been reported.

The major aim of research in cancer chemotherapy is to develop a drug or drugs which will not only produce general improvement in patients with malignant tumors but will also irrevocably destroy the tumors. While numerous compounds exist which will kill living tumor cells, most of them are not selective enough to accomplish this feat without damaging normal cells as well. Some drugs such as the alkylating agents (nitrogen mustard, triethylenemelamine, triethylenephosphoramide, and triethylenethiophosphoramide among them) are effective and reasonably safe, because the rapidly multiplying cells of tumors are more susceptible to their cytotoxic effect than are normal cells. Other agents (the antimetabolites) retard the growth of tumors by interfering selectively with certain metabolic pathways within the tumor cells [*1,2*]. The effective agents may produce temporary reduction in the mass of the tumor, but in time it breaks loose from this control and resumes its unhampered growth until it kills the patient. The development of resistance to a drug is explained on the basis of recovery from the cytotoxic effect and the ability of the cancer cells to utilize other metabolic pathways which are not blocked by the drug.

Ordinarily a tumor which has been inhibited by a chemotherapeutic agent gives histologic evidence of partial destruction, but later, when the resistance to the agent has developed, the tumor grows again and biopsy reveals a return to its histologic appearance before treatment. It is unusual to see the permanent destruction of a tumor by chemotherapy. Although this phenomenon has been reported for some types of tumors treated with various chemotherapeutic agents [*3,4*], search of the literature fails to reveal a report of malignant melanoma which has been permanently destroyed in one area by local treatment with triethylenethiophosphoramide [*5,6*].

It is the purpose of this report to present the interesting observation of the "permanent" destruction of a nodule of malignant melanoma by the chemotherapeutic injection of triethylenethiophosphoramide (Thio-TEPA) directly into the tumor.

CASE REPORT

A seventeen year old white schoolboy (N.Y.H. No. 714318) was admitted to The New York Hospital for the first time on June 29, 1955, with the chief complaint of a mass behind the left ear. In February, 1955, a small nevus behind the left ear, which had been present since birth, was accidentally traumatized and bled slightly. It began

to grow and after two months was excised locally at another hospital. The diagnosis was malignant melanoma but no further treatment was recommended. In May a small, painless nodule appeared in the scar and began to enlarge slowly. It was for the excision of this nodule that hospitalization was advised.

On admission to The New York Hospital the physical examination was unremarkable except for a small nodule in the left postauricular scar and the presence of a palpable posterior cervical lymph node. A left radical neck dissection was carried out in continuity with wide excision of the postauricular skin and subcutaneous tissue. A split-thickness skin graft was used to close the postauricular wound. Histologic examination revealed malignant melanoma with cervical lymph node metastasis. The postoperative course was uneventful and the patient was discharged from the hospital but returned with several subcutaneous nodules in the left side of the neck. A course of x-ray therapy (3,700 r) was given to this area but it was entirely ineffectual in arresting the growth of any of the lesions.

On February 2, 1956, triethylenethiophosphoramide (Thio-TEPA) 15 mg. was injected into a blue nodule in the left supraclavicular area. Within one week the injected nodule diminished in diameter from 1.5 to 1.0 cm. There was no change in the other uninjected nodules in the vicinity. On February 18th and 25th, 10 mg. of Thio-TEPA were injected into the same lesion. On February 25th an additional 10 mg. of Thio-TEPA was given intramuscularly. Intramuscular administration was continued in doses of 10 to 30 mg. at about weekly intervals for the next three months for a total dose of 160 mg. Temporary arrest of the growth of all the nodules occurred. At the end of this three-month period, however, the progressive growth of the tumors resumed with the exception of the mass which had been injected locally with the drug. This lesion remained 1.0 cm. in diameter until the patient's death. A new nodule appeared over the left scapula and Thio-TEPA was injected into this weekly for a total dose of 55 mg. Although the nodule did not decrease in size, it did not grow any larger during the remainder of the patient's life.

The patient's general condition remained satisfactory but his white blood cell count fell to 2,750 per cu. mm. by July 20, 1956. Metacortin® 10 mg. per day was given for seven days. After this therapy the leukopenia was less marked.

In August, 1956, while on a European tour, the patient experienced nausea, vomiting, malaise, anorexia and fever, followed within a week by orange discoloration of the urine and generalized icterus. He returned to New York and was readmitted to the hospital. There was no history of blood transfusion or of contact with a patient with jaundice. Positive physical findings were generalized icterus, the liver edge palpable at the costal margin, and intracutaneous blue-black nodules in the left postauricular area under the angle of the left mandible and along the anterior border of the left trapezius muscle. There were also firm, immovable subcutaneous masses along the border of the trapezius, around the left temporomandibular joint and over the left sternoclavicular joint. There was moderate trismus and pain in the left temporomandibular joint when the patient attempted to open his mouth. Because of a markedly elevated serum transaminase (1,164 units) the diagnosis of viral hepatitis was made. On bed rest and supportive therapy the serum bilirubin fell to normal and the patient's general condition improved. One of the submandibular nodules on the left side of the neck was biopsied and it revealed malignant melanoma. Attempts to grow this tissue by tissue culture technics were unsuccessful.

Because of the development of a painful mass below the right knee, an x-ray film was taken. This revealed extensive destruction of the upper end of the tibia, presumably by a large metastatic lesion. A roentgenogram of the chest was normal.

On August 31, 1956, actinomycin D therapy was started in the hope of arresting the growth of the metastases. This drug was administered intravenously in the dose of 650 gamma every other day for a total dose of 6,500 gamma. On this therapy there was progressive but moderate diminution of the platelet count, and some malaise and anorexia a few hours after each dose. However, the pain in the left mandible diminished and the patient was able to open his mouth much further than he could before treatment. A course of x-ray therapy to the metastasis in the right tibia was begun on October 3rd. A total of 300 r was given over a two-week period, with complete relief of pain in this area, although the mass did not change in size.

A second course of actinomycin D was begun on October 6th but this was poorly tolerated, and after 4,000 gamma failed to produce any apparent beneficial effect the drug was discontinued. An additional 85 mg. of Thio-TEPA was given intramuscularly in November and December, 1956, but no improvement was noted. The patient's general condition gradually deteriorated and he died at home on January 4, 1957.

An autopsy was performed at the Greenwich Hospital, Greenwich, Connecticut. The positive findings were as follows: On the left side of the neck were healed scars of radiotherapy and the radical neck dissection. In the same region were multiple firm intracutaneous and subcutaneous nodules extending from the angle of the left mandible upward to the postauricular area. On the left side of the chest, just lateral to the nipple,

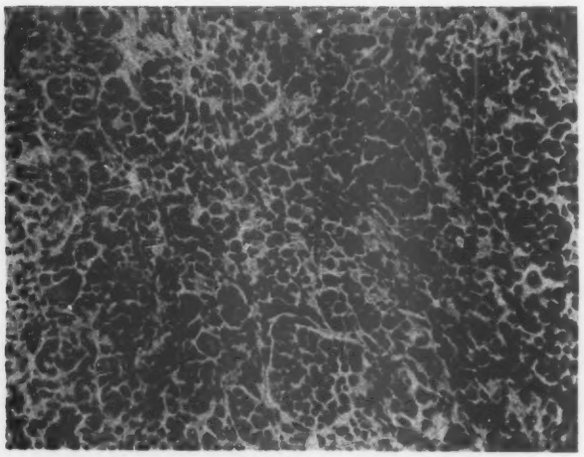

FIG. 1. Metastatic malignant melanoma in lymph node in left side of neck. No local Thio-TEPA. × 200.

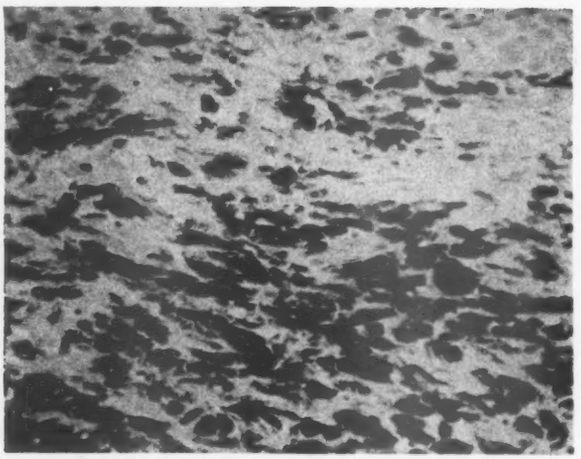

FIG. 2. Metastatic malignant melanoma in skin of left side of neck eleven months after local injection of Thio-TEPA. Note melanin in macrophages and fibroblasts but absence of neoplastic cells. Original magnification × 330.

was a 2 by 2 cm. blue-black subcutaneous tumor. A similar slightly larger nodule was noted over the right sixth rib in the anterior axillary line. Along the anterior margin of the left trapezius was a matted mass of nodes, with several black intracutaneous nodules. At the base of the neck was one firm mass with a pale contracted scar over it. This represented the lesion which had been treated with local Thio-TEPA.

Several small bluish areas were noted in the diplöe of the skull. The brain was extremely swollen, softer than normal, and weighed 1,680 gm. The sulci were almost obliterated and the gyri were flattened. On section a 6 by 6 cm. tumor was noted in the right frontal lobe. The lesion was soft, irregular and reddish black; the brain surrounding it was yellow and necrotic. After the brain had been removed, the area of the pituitary was seen to contain a large black mass which had destroyed the pituitary gland and a considerable part of the sella turcica and had eroded into the sphenoid sinus. After fixation the sectioned brain showed smaller black nodules, ranging in size from 0.3 to 1.2 cm., in the right and left parietal lobes, the medulla and the cerebellum. In the sternoclavicular region was a large black tumor replacing the medial end of the clavicle and the manubrium of the sternum. The fifth dorsal vertebra, the upper end of the right tibia and the ascending ramus of the left mandible also contained friable black neoplastic tissue.

There were several black subepicardial nodules of tumor on the surfaces of the two auricles of the heart and a tumor-filled lymph node between the left auricle and the adventitia of the great vessels.

Multiple metastases, ranging in size from 0.3 to 3.0 cm., were found in the upper lobe of the right lung, the lower lobe of the left lung, the spleen and the liver.

The gastrointestinal tract, pancreas, adrenals, kidneys and urinary bladder showed no abnormalities.

Histologically almost all the nodules of tumor appeared the same. The cells were very pleomorphic but were easily recognized as those of malignant melanoma. (Fig. 1.) Mitoses were present but were not numerous. There was a great deal of intracellular melanin in the tumor cells and this was present also in chromatophores of the stroma. Occasional multinucleated giant cells were seen.

Attempts to grow the tumor in tissue culture were again unsuccessful.

Of particular interest was the subcutaneous lesion at the base of the left side of the neck which had been treated by local injection of Thio-TEPA. Grossly this mass was black and looked exactly like the other lesions. However, microscopically it was found to consist mainly of fibrous tissue, with abundant melanin pigment incorporated in the fibroblasts and in macrophages between the fibrous strands. *No neoplastic cells were seen in the lesion.* (Fig. 2.)

COMMENTS

This case presents the typical picture of recurrent malignant melanoma. The feature of interest is the local effect of triethylenethiophosphoramide (Thio-TEPA) on a test nodule of metastatic tumor. The drug injected directly into the nodule produced a fairly prompt reduction in its size. Concurrently there was a slight reduction in the size of the surrounding metastatic lesions while the patient was receiving the drug systematically. When the tumor developed resistance to the drug after about three

months, all the lesions again began to grow, new metastases appeared throughout the body and the patient died of the disease. However, the lesion that had received the drug locally did not grow in the remaining eleven months of the patient's life, and at autopsy this nodule was seen to contain melanin pigment but no viable, neoplastic cells.

The nodule in the neck which was treated with local Thio-TEPA was within the area which had been treated by x-ray therapy. However, the nodules of tumor which surrounded this lesion, and also treated by x-ray therapy but not by local injection of Thio-TEPA, had continued to grow and at autopsy were still histologically typical, unaltered, malignant melanoma.

SUMMARY

A case of recurrent malignant melanoma is presented. Temporary arrest of the growth of metastatic nodules was accomplished with the systemic administration of triethylenethiophosphoramide (Thio-TEPA). The only nodule whose growth was permanently arrested was one that had been locally injected with Thio-TEPA. Histologic examination of this nodule at autopsy revealed the absence of viable tumor cells, although there was abundant melanin in fibroblasts and macrophages.

Acknowledgment: The authors are grateful to Dr. Jane C. Wright and her staff of the Fourth Surgical Division, Bellevue Hospital, New York City, for managing the chemotherapy in this patient, and to Dr. Joyce Morris, Pathologist at the Greenwich Hospital, for performing the autopsy.

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Cecal Carcinoma Masked by Acute Appendicitis

WOLFGANG H. MARKGRAF, M.D., *Bay Pines, Florida*

From the Surgical Service, Veterans Administration Center, Bay Pines, Florida.

CARCINOMA of the cecum as the etiology of appendiceal perforation is often overlooked.

It is realized that acute appendicitis may simply be concomitant to carcinoma of the cecum. It is well recognized, however, that obstruction of the appendix is most frequently the etiological factor in acute appendicitis. Collins [1] reported obstruction in 50 per cent of a series of 3,400 cases of acute appendicitis.

The pathogenesis of the clinical association under consideration is believed to result from obstruction of the lumen of the appendix or the lumens of the lymphatics and/or the blood vessels by carcinoma cells. Erosion of the surface of the carcinoma and bacterial extension into the cecum and appendix is another possibility, as mentioned by McLaughlin [2].

Most recent reports on this syndrome are by Miller and Wooldridge [3] who reported a case in 1954 in which the diagnosis was made by microscopic examination of material taken from a pericecal abscess. Robinson and Ernst [4] reported a case in 1953. They reviewed the world literature finding nineteen cases, and added one of their own. Patterson and Deavers [5] reported that three of twenty-nine cases of a series of carcinoma of the cecum had proved acute appendicitis as a complication of their cecal malignancy. Patterson [6] reported thirteen cases of cecal carcinoma in which the base of the appendix was blocked, resulting in acute appendicitis. He makes a plea for primary resection.

The importance of recognizing this condition is borne out by Ransom [7] in a review of carcinoma of the right colon. He states that 10 to 15 per cent of patients who came to surgery for carcinoma of the right colon had undergone a preliminary appendectomy. This would imply that surgeons often overlook the possibility of an underlying carcinoma of the cecum presenting as acute appendicitis.

The opportunity for diagnosis and cure is afforded at the operating table through teamwork between the surgeon and pathologist. The surgeon should examine the cecum in every appendectomy even though he is reluctant to spread contamination from a localized abscess or perforated appendix. A necessary prerequisite for the thorough examination of the cecum during appendectomy is an adequate (McBurney)* incision. The keyhole incision is to be condemned. If inflammatory induration of the cecum is so marked that neoplasm cannot be ruled out, cecotomy for visualization, palpation and biopsy are recommended. This direct examination of the indurated cecum may enable the surgeon well trained and experienced in gross pathology to make a diagnosis. Microscopic examination, however, may be the only means of establishing the diagnosis and may make the difference between a radical curative operation at the time, or a delay sufficient to allow the tumor to metastasize. When the surgeon is suspicious of malignancy, microscopic examination can dispel any fear of closing the abdomen in the presence of a resectable lesion, or can strengthen his conviction for a radical curative procedure.

Three cases of this interesting clinical problem have come to our attention in the past two years at the Coral Gables Veterans Administration Hospital. This is an indication of the frequency of this occurrence. The first such case was reported by us recently [8]. The other

* Whether a McBurney incision will always be adequate is open to question. Certainly if a carcinoma is discovered, the McBurney incision had best be closed and another incision made which is adequate for hemicolectomy.

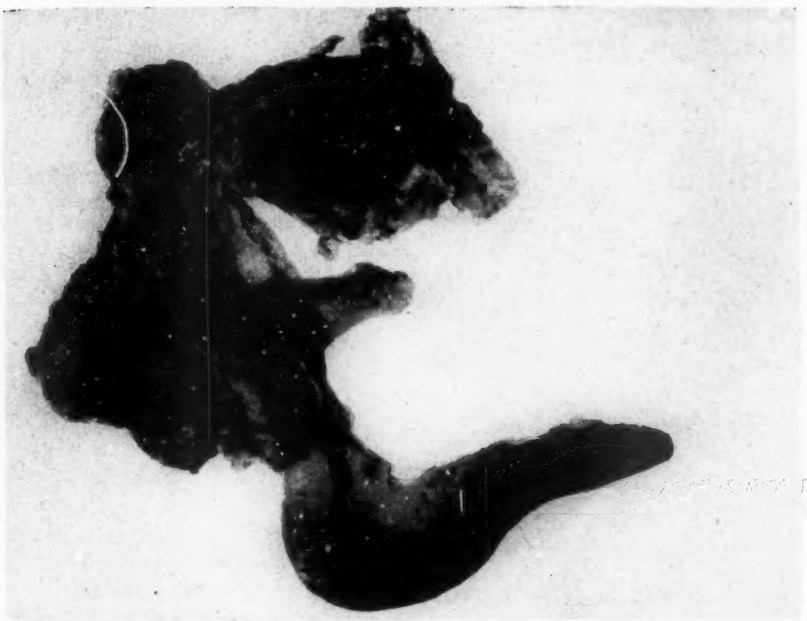

FIG. 1. Case I. Shows resected specimen with lumen of appendix surrounded by tumor tissue. The cecum has been opened.

two additional cases demonstrate the clinical problem and the extremes of success and failure in handling them.

CASE REPORTS

CASE I. H. E. D. (No. 51 866), a seventy year old white man was admitted on September 1, 1955, with a history of mid-epigastric pain of two weeks' duration, suddenly becoming quite severe. Examination revealed board-like abdominal rigidity and generalized tenderness. The upright chest films showed right subdiaphragmatic air. A diagnosis of perforated peptic ulcer was made. At operation a perforated duodenal ulcer was found and closed. Exploration revealed a mass at the ileocecal junction. Blunt dissection freed the ileum which was wrapped about the appendix which had perforated. A lesion was palpated in the cecum and was considered to be malignant. Cecotomy and biopsy for frozen section was accomplished. Frozen section confirmed the suspicion of malignancy and a right hemicolectomy was performed with ileotransverse colostomy.

Grossly, the posterior wall of the cecum was infiltrated by a 2 by 3 cm. mass of firm, friable tumor tissue which involved the mucosa and muscularis and protruded into the lumen. (Fig. 1.) The appendix was fragmented and the base appeared involved by tumor which was continuous with the cecal mass.

Microscopically, sections from the tumor showed atypical glands with large and bizarre epithelial cells which infiltrated all portions of the bowel wall. Sections from the appendiceal stump showed infiltration of the muscular layer by tumor. There was considerable necrosis in this area, together with infiltration by mixed inflammatory cells, chiefly by histiocytes.

FIG. 2. Case II. Shows cross section of appendix removed at first operation.

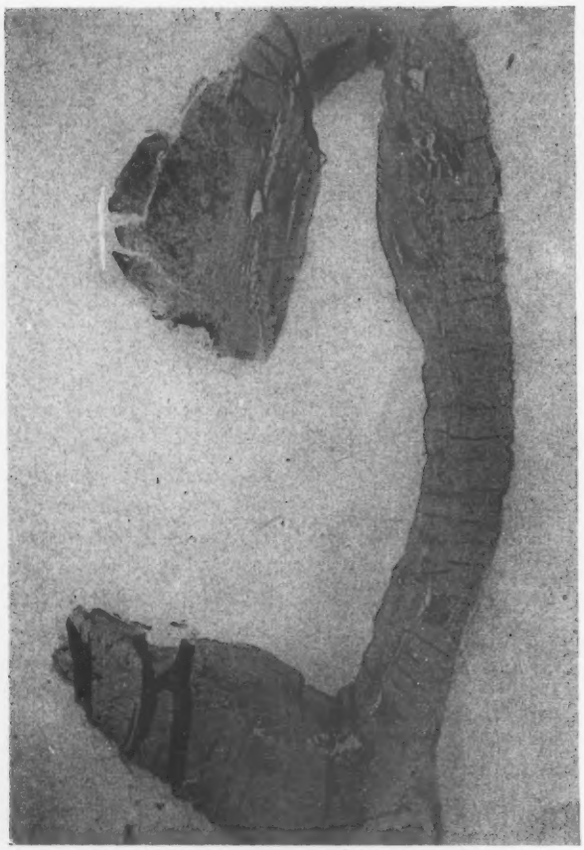

FIG. 3. Case III. Shows cross section of mid-portion of appendix; carcinoma of gallbladder metastatic to appendix.

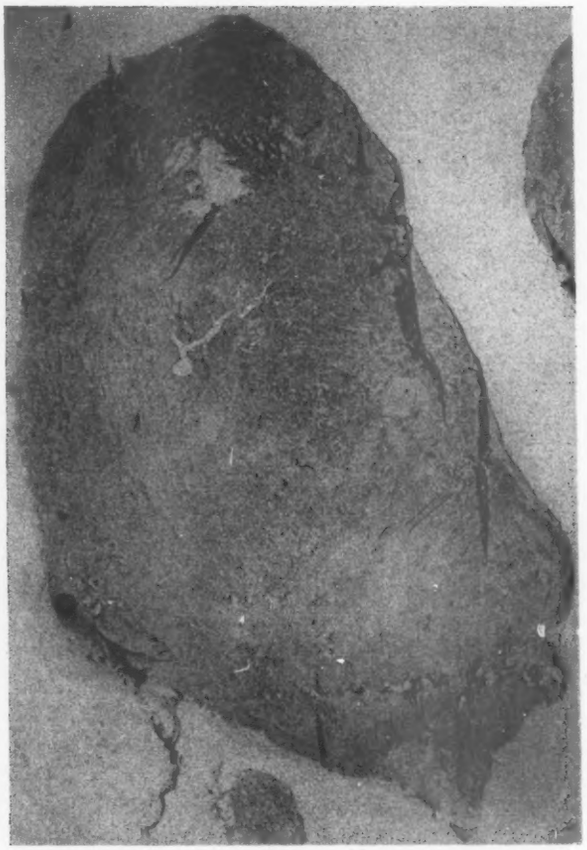

FIG. 4. Case III. Shows tip of appendix with lumen almost obliterated by metastatic tumor.

CASE II. W. H. C. (No. 51 416), a forty-two year old white man was admitted on December 17, 1955. He had had an appendectomy in another hospital in August, 1955, because of acute abdominal pain. The pathologist reported subacute appendicitis and periappendicitis. (Fig. 2.) Postoperatively the patient continued to have his abdominal complaint and because of the marked induration of the cecum found at surgery, a follow-up examination was done with barium enema. A filling defect of the cecum was reported. This was interpreted as inflammatory and the patient was given a course of emetine followed by metacortin.®

The patient was admitted to our hospital in December, 1955. A fresh perspective could only permit a diagnosis of carcinoma. Exploratory laparotomy revealed far advanced carcinoma of the cecum with metastases. An ileotransverse colostomy for by-pass was performed. The patient died of his disease in March, 1956. Microscopic section from the mesentery showed metastatic adenocarcinoma, large bowel type.

CASE III. We also have a case coming to autopsy for carcinoma of the gallbladder which coincidentally showed involvement of the appendix. Although death intervened before perforation occurred, we believe that this involvement of the appendix by carcinoma shows the pathogenesis of perforation of the appendix in such a situation.

At autopsy there was an ulcerated umbilical tumor of the cecum measuring 3½ cm. in diameter. This extended through the wall into the mesentery. Just immediately adjacent, the opening of the appendix was completely obliterated by a similar yellowish tumor which completely infiltrated the wall of the appendix for a distance of 1 cm. in the region of the neck. The lumen here was completely obliterated. Distal to this the wall of the appendix was thin and the lumen greatly dilated to approximately 1½ cm. in diameter and filled with a liquid greyish yellow exudate. The mucous membrane otherwise appeared normal. However the tip of the appendix was occupied by a nodular, mottled, yellowish red tumor mass, which again completely obliterated the lumen of the appendix. This mass measured approximately 1½ cm. in diameter.

Microscopically, section from the base of the appendix showed extensive invasion of the submucosa and muscularis by adenocarcinoma. There

was much atrophy of the lymphocytic tissue and the mucosa had practically disappeared. Section through the mid-portion of the appendix again showed severe atrophy of the lymphatic tissue and mucosa with focal areas of metastatic carcinoma of the muscularis. (Fig. 3.) Section from the tip of the appendix again showed severe compression of the lumen with atrophy of mucosa and lymphoid tissue by extensive nodular infiltration of the muscularis and submucosa by metastatic adenocarcinoma (Fig. 4.)

SUMMARY

In conclusion, the surgeon should consider diagnosis of carcinoma of the cecum in acute appendicitis, especially in the presence of a mass in the right lower quadrant of the abdomen. The diagnosis is difficult to make preoperatively. The surgeon should examine the cecum in every appendectomy. If a questionable mass is present, cecotomy for palpation and/or biopsy for frozen section is recommended. Keyhole incision for appendectomy should be condemned inasmuch as this does not allow adequate visualization of the cecum. The patient should be examined by means of a barium enema if there is any question following appendectomy. A "second look" operative procedure when any doubt remains is more conservative than procrastination. Persistent sinuses or fecal fistulas following drainage of an appendiceal abscess are warning signals. A persistent mass in the right lower quadrant of the abdomen following appendectomy should arouse suspicion of carcinoma. Anemia in the presence of the aforementioned findings increases the likelihood of carcinoma. Early surgery is the only hope for cure. A right hemicolectomy should be performed if carcinoma of the cecum is found during appendectomy.

Acknowledgment: The author acknowledges with thanks the assistance of the Department of Pathology and the Photographic Laboratory of the Veterans Administration Hospital, Coral Gables, Florida.

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Diverticulitis of the Cecum Simulating Appendicitis

LAWRENCE SINGMASTER, M.D., *Philadelphia, Pennsylvania*

From the Surgical Service, Lankenau Hospital, Philadelphia, Pennsylvania. Presented before the Philadelphia Academy of Surgery, May, 1957.

TWO patients with diverticulitis of the cecum have recently been operated upon at the Lankenau Hospital with a preoperative diagnosis of acute appendicitis having been made in each case. Owing to the relative infrequency of diverticulitis simulating appendicitis, we believe that these instances are worthy of recording.

CASE REPORT

CASE I. A fifty-seven year old white woman was admitted to the hospital on March 23, 1957, complaining of abdominal discomfort. The duration of symptoms was approximately six hours, and pain was most prominent in the right lower abdominal quadrant. The pain was characterized as being sharp, constant and aggravated by walking or standing. There was also a history of recent slight constipation and the patient had had a bowel movement twenty-four hours before admission. There had been no melena, however, and the consistency and caliber of the stools had not changed. Anorexia had been present for six hours but the patient only suffered slight nausea and no vomiting had occurred.

The past medical history revealed no previous operations or serious illnesses and the systemic review was non-contributory except for mild hypotension without symptoms.

Physical findings demonstrated an alert white female patient with apparent abdominal distress. The blood pressure was recorded at 92/62 mm. Hg, the pulse was 96, respirations 20 and temperature 101°F. Abdominal examination revealed marked tenderness over McBurney's point with muscle guarding and rebound tenderness extending slightly into the right flank. There was no abdominal distension, no masses were palpable, and peristalsis was audible but hypoactive. There was no costovertebral angle tenderness bilaterally and pelvic and rectal examinations revealed no abnormalities.

Laboratory studies included a red blood cell count of 4,900,000 per cu. mm. with 14.3 gm. hemoglobin. The white blood cell count was 10,500 cells per cu. mm. of which 75 per cent were neutrophils, 18 per cent lymphocytes, 6 per cent monocytes and 1 per cent eosinophils. The urinalysis was within normal limits.

A tentative diagnosis of acute appendicitis was made and the patient was prepared for surgery. The abdomen was entered through a right McBurney incision and the appendix was found to be grossly normal. Palpation of the cecum revealed an inflammatory mass to be present on its anterior surface approximately 6 cm. at its greatest diameter. The McBurney incision was then closed and the abdomen was reopened through a large right paramedian incision. Adequate exposure was thereby obtained and the cecal mass was thought to be either a perforating diverticulum or a neoplasm. No evidence of gross metastases was apparent. Right colectomy was then performed removing a small portion of the terminal ileum, the right colon and one-third of the transverse colon. An ileotransverse colostomy was then effected and the operation concluded. The patient tolerated the operation well and was discharged twelve days following surgery and an uneventful convalescence.

Pathological examination of the specimen revealed an acute diverticulitis of the cecum with abscess formation and the appendix presented acute periappendicitis. This patient has been seen for follow-up purposes on three occasions and is in excellent health, bowels moving once daily. She has resumed her normal activities.

CASE II. A fifty-seven year old white woman was admitted to the hospital on August 27, 1956. This patient had been well until one and a half days prior to admission when she noticed vague epigastric discomfort. This discomfort persisted for twenty-four hours despite home remedies when she was seized with sharp pain in the right lower abdominal quadrant. The pain was most marked on moving, and on examination by her family physician the right lower abdomen was very tender to

palpation. There had been no nausea or vomiting. Bowel habits had not changed and the systemic review was non-contributory.

The past medical history revealed no previous operations or serious illnesses.

On admission the blood pressure was recorded at 130/80 mm. Hg, pulse 74, respirations 20, and temperature 100°F. Findings of note were confined to the abdomen where there was marked pain to palpation in the right lower quadrant of the abdomen, rebound tenderness and muscle guarding. Peristalsis was audible and no distension or masses were apparent. There was no costovertebral angle tenderness and pelvic and rectal examinations revealed no abnormalities.

Blood studies demonstrated 14.4 gm. hemoglobin, 42 volumes per cent microhematocrit, 10,800 white blood cells per cu. mm. with 84 per cent neutrophils, 14 per cent lymphocytes and 2 per cent monocytes. The urinalysis revealed a trace of albumin but was otherwise within the limits of normal.

The tentative diagnosis of acute appendicitis was made and the patient underwent surgery. The operation closely resembled the previous case in that a large tumor of the cecum was identified through a McBurney incision. This incision was closed and proper exposure was obtained through a right paramedian incision. The mass in the cecum was approximately 2 cm. from the appendix and was grossly inflammatory being 4 cm. at its greatest diameter. The clinical impression was that this represented either a perforating diverticulum or a neoplasm. No evidence of gross metastases was apparent and right colectomy was performed in a similar fashion to the previous case. The convalescence was uneventful and the patient was discharged ten days following surgery. The patient has been seen on two occasions since surgery and was in good health having normal bowel movements and no abdominal complaints.

The pathological diagnosis of the specimen was acute diverticulitis of the cecum with abscess formation and acute periappendicitis.

COMMENTS

Diverticulitis of the cecum is by no means a rare entity as evidenced by the fact that 166 cases have been reported in the literature [*1*]. It is the consensus of opinion of numerous authors that should a large inflammatory mass be encountered, right colectomy should be performed. If a perforating lesion with peritonitis is present, however, it is recommended that adequate drainage be established and definitive resection be performed at a later date. In very small diverticular lesions some authors have recommended simple inversion or local excision of the area involved.

We strongly recommend right colectomy in the larger inflammatory lesions owing to the difficulty in differentiating between benign and malignant tumors in the majority of such cases. Owing to the acute nature of the presenting symptoms and objective findings in the two cases just presented, additional studies such as barium enema x-rays were considered to be contraindicated and, indeed, dangerous.

CONCLUSIONS

Diverticulitis of the cecum can easily be confused with acute appendicitis and the surgeon should be prepared to perform a right colectomy if a large inflammatory mass is encountered. If frank perforation or peritonitis is present, however, adequate drainage followed by later resection is recommended.

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Strangulated Partial Enterocele Involving Cecum in a Femoral Hernia

WILLIAM A. DWYER, JR., M.D. AND GEORGE M. SAYPOL, M.D., *New York, New York*

From the Department of Surgery, New York University Post-Graduate Medical School, New York, New York.

RECENTLY a strangulated femoral hernia involving a portion of the wall of the cecum focused our attention on the problem of Richter's hernia and stimulated a search of the literature. No similar case was found [*1–25*].

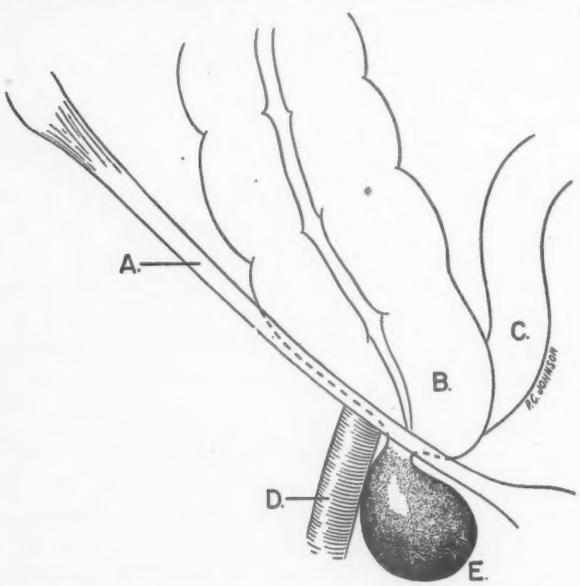

FIG. 1. Shows strangulated hernial mass. A, inguinal ligament; B, cecum; C, ileum; D, femoral vein; E, strangulated mass.

Richter's hernia (or partial enterocele) is described as a protrusion of a portion of the bowel circumference into one of the orifices of the abdominal wall [*12,20*]. The orifice most frequently involved is the femoral ring, with the ileum being the most common segment of gut involved. Isolated cases of Richter's hernia have been described involving the ascending colon and cecum in inguinal hernias [*6,15*]. Several cases of partial enterocele in ventral hernias have also been described [*9*].

It is estimated that Richter's hernia comprises 0.7 per cent of all femoral hernias [*20*] and 10 per cent of all strangulated femoral hernias [*25*]. Because of the deceptively mild symptoms associated with it and the absence of signs of complete obstruction despite strangulation, these cases are frequently misdiagnosed and operative treatment is delayed. As a result, there is a concomitant high mortality rate for what should be a surgically remediable lesion. In two recent series (Bellevue Hospital, 1948 [*19*]; Wayne County Hospital, 1956 [*22*]) the mortality rate is quoted as 33 per cent.

CASE REPORT

A forty-seven year old white woman (L6414) was admitted on May 11, 1957, to the University Hospital with a diagnosis of incarcerated right inguinal hernia. She stated that at intervals for the past several years she had noted a mass in the right groin. This had been diagnosed by various physicians as an enlarged lymph node or a varicose vein. Approximately twenty-four hours prior to admission she noted the sudden onset of pain in this mass, accompanied with a waxing and waning soreness in the lower abdomen. She was not sufficiently uncomfortable to call a physician. On arising the following morning, however, she found the mass to be still present and painful. She consulted her physician, who made an unsuccessful attempt at manual reduction and then advised hospitalization.

During this twenty-four hour period she had not felt hungry and consequently had eaten nothing except some coffee and toast on the morning of admission. At no time had she vomited, nor did she feel nauseated. She had had a normal bowel movement during the twenty-four hours preceding admission but subsequently had not passed gas.

A review of systems revealed no abnormality except for dyspnea on moderate exertion. Her past

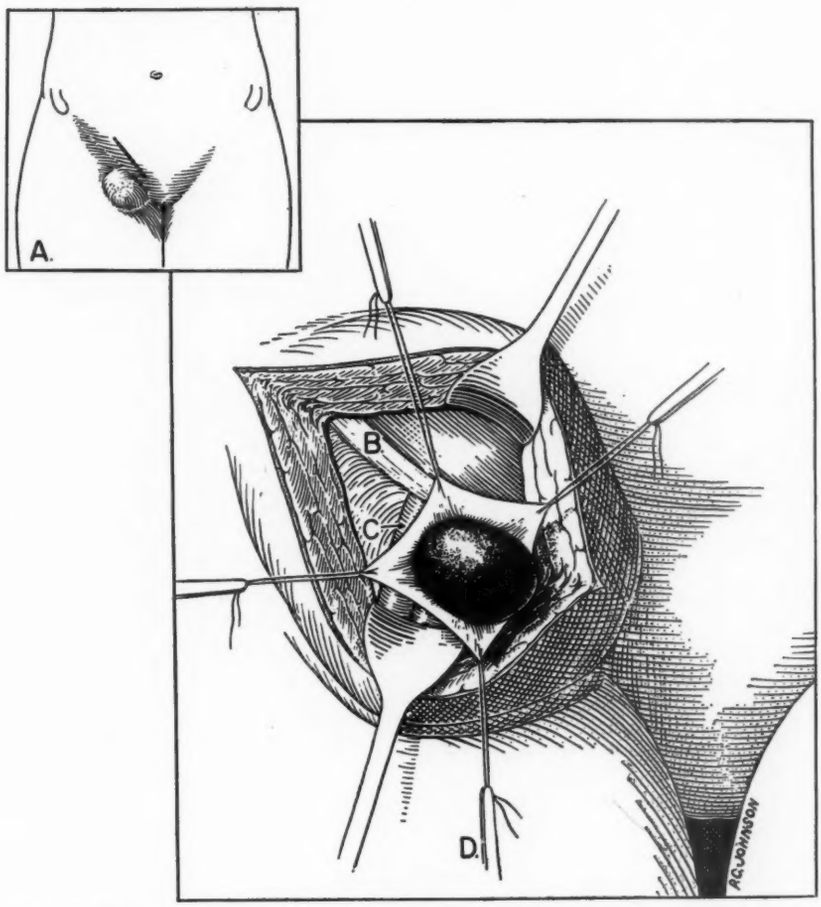

FIG. 2. Shows gangrenous cecal wall through opened hernial sac. A, inset: incision; B, inguinal ligament; C, femoral artery; D, wall of hernial sac.

medical history was significant only in that she had had rheumatic heart disease for the past twenty-five years and poliomyelitis as a child.

Physical examination revealed a well nourished, well hydrated white woman who was in no distress. Her temperature was 37.8°C. She had a loud clicking second sound at the mitral area. The abdomen was not distended; there was no guarding or rigidity and there were no hyperactive bowel sounds on auscultation. In the right groin (Fig. 1A) there was a 3.0 by 3.0 by 4.0 cm. exquisitely tender mass which appeared to extend upward from the femoral triangle medial to the vessels in the region of the external inguinal ring.

Laboratory findings showed a hemoglobin of 12.8 gm. per cent, red blood cell count of 4.57 million per cu. mm., white blood cell count of 17,500 per cu. mm., segmented neutrophils 85 per cent, lymphocytes 13 per cent and monocytes 2 per cent. Scout films of the abdomen showed only some gaseous distention of the large bowel.

Operation was performed within four hours of admission. An incision was made paralleling the right inguinal ligament, and the external oblique fascia was incised. The femoral sac was opened and a 4 cm. segment of gangrenous cecal wall was found. (Figs. 1 and 2.) This proved to be part of the anteroinferior portion of the cecum. The fossa ovalis was enlarged and the hernial sac and its bowel content passed beneath Poupart's ligament, converting the hernia into a direct inguinal hernia. A rubber-shod clamp was then utilized to exclude the gangrenous segment from the remainder of the gastrointestinal tract and the devitalized segment was excised longitudinally. The defect in the cecum was closed transversely and returned to the peritoneal cavity. Cooper's ligament was then sutured to the shelving edge of Poupart's ligament, following which a Bassini type closure was performed.

The patient's postoperative course was satisfactory except for moderate serosanguineous drainage from the wound between the fifth and twelfth postoperative days. She was discharged from the hospital on the eighth postoperative day.

SUMMARY

The authors' experience with an apparently unique case of Richter's hernia is presented.

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Leiomyosarcoma of the Ascending Colon Associated with Multiple Polyposis

DONALD F. GUISTO, M.D., *Reno, Nevada*, MORTON J. THOSHINSKY, M.D., *San Francisco, California*, AND LOUIS G. BRIZZOLARA, M.D., *Mill Valley, California*

WE believe this to be the first reported case of leiomyosarcoma of the large bowel associated with multiple polyposis. Leiomyosarcomas of the large bowel, exclusive of the rectum, are quite rare. Search of the literature reveals only fourteen reported cases, and this is submitted as the fifteenth case of leiomyosarcoma of the large bowel and the first case of leiomyosarcoma associated with multiple polyposis. (Table 1.)

The clinical picture and pathological findings of these tumors of the large bowel were reviewed by MacKenzie, McDonald and Waugh in 1954 [2], and more recently by Morton, Stabins and Morton in 1956 [4].

CASE REPORT

This twenty-seven year old white man was first admitted to the San Francisco Veterans Administration Hospital (HSH-87345) July 19, 1956, with a complaint of diarrhea of four months' duration.

Review of the past history revealed that the patient had had pain in the right lower quadrant of the abdomen for two weeks in December, 1955, at which time a diagnosis of appendicitis was made. Appendectomy was performed; however no tumor mass was noted at the time of surgery. For the four months prior to his admission, the patient had had persistent diarrhea consisting of four to five loose stools per day. Stools were associated with a marked degree of flatulence but there was no evidence of bleeding. The patient felt generally run down with malaise associated with shortness of breath. His general condition was otherwise good. He had no recent weight changes. He maintained his appetite and had no history of nausea and vomiting.

Positive physical findings were limited entirely to the abdomen. A well healed right McBurney

TABLE 1

REPORTED CASES OF LEIOMYOSARCOMA OF THE LARGE BOWEL EXCLUSIVE OF RECTUM

Reference	Age (yr.) and Sex of Patient	Location of Tumor
Scott, 1923 [7]	16, M	Hepatic flexure
Trygstad, 1932 [8]	19, M	Cecum
Neugebauer, 1932 [5]	48, F	Cecum
Golden and Stout, 1941 [1]	78, M	Sigmoid colon
Golden and Stout, 1941 [1]	47, M	Descending colon
Ripstein and Flint, 1952 [6]	56, F	Cecum
Mackenzie, McDonald and Waugh, 1954 [2]	Not stated	Ascending colon
Mackenzie, McDonald and Waugh, 1954 [2]	Not stated	Transverse colon
Mackenzie, McDonald and Waugh, 1954 [2]	Not stated	Transverse colon
Mackenzie, McDonald and Waugh, 1954 [2]	Not stated	Sigmoid colon
Mackenzie, McDonald and Waugh, 1954 [2]	Not stated	Sigmoid colon
Marshall and Cherry, 1955 [3]	41, M	Sigmoid colon
Marshall and Cherry, 1955 [3]	43, F	Transverse colon
Marshall and Cherry, 1955 [3]	60, F	Sigmoid colon
Guisto, Thoshinsky, Brizzolara	27, M	Ascending colon associated with multiple polyposis

FIG. 1. Barium enema demonstrating lesions of ascending colon, splenic flexure and sigmoid colon.

FIG. 2. Leiomyosarcoma involving ascending colon. Cross section showing main lesion and subserosal metastasis.

scar was noted overlying a freely movable, slightly tender mass. Bowel sounds were active and there was no evidence of distention. Rectal examination was negative, but on sigmoidoscopy to 25 cm. several small sessile polyps, ranging in size from 2 mm. to 4 mm. in diameter, were noted.

The initial hemoglobin determination revealed an anemia of 6 gm. per 100 cc. Stools were consistently positive for occult blood. Total protein, albumin-globulin ratio, and prothrombin time were within normal limits. X-ray of the chest was within normal limits. Barium enema revealed three large polypoid masses. The largest mass was in the area of the ascending colon; of the two smaller masses, one was in the splenic flexure and one in the sigmoid colon. (Fig. 1.)

The patient received multiple blood transfusions and was prepared for surgery. On August 6, 1956, he was taken to the operating room and under general anesthesia, with ureteral catheters in place, the abdominal cavity was entered through a left rectus incision. Abdominal exploration revealed a large lobulated mass approximately 10 by 10 by 12 cm. involving the mid-ascending colon. In addition to this mass, two smaller polypoid masses could be felt in the distal colon, one just below the splenic flexure and a second in the upper sigmoid. There was no evidence of metastases to the liver or to the regional lymph nodes. Subtotal colectomy was then performed, anastomosing the terminal ileum to the upper rectum, so that the remaining large bowel could be inspected through the sigmoidoscope.

Postoperatively the patient did well. The cotton skin sutures were removed on the seventh postoperative day and the twisted steel wire retention sutures removed on the fourteenth postoperative day. The patient was then given a low residue diet and discharged from the hospital.

The gross pathological findings (Figs. 2 through 6) indicated that the specimen consisted of 2 cm. of terminal ileum, the cecum and entire colon to the rectosigmoid. It measured 122 cm. in length in the fixed state. In the lumen of the ascending colon, 11 cm. distal to the ileocecal valve, was a large, solid, polypoid tumor measuring 3½ cm. by 7½ cm. by 11 cm. Its consistency was firm, and the mucosal surface was granular and ulcerated. On cut section, the tumor was grey-white in color with areas of hemorrhage, and appeared to arise from the muscular layers. A separate tumor nodule was noted in the subserosal fat, measuring 4 cm. in diameter subjacent to the main tumor. (Fig. 2.) The main tumor almost occluded the lumen of the bowel.

Two other lesions, both rising some 3 cm. above the mucosa and 6 cm. in diameter were noted, one in the splenic flexure and the other in the sigmoid colon. (Fig. 3.) The remainder of the bowel was studded with small sessile polyps measuring 2 to 6 mm. in diameter. (Fig. 4.)

Microscopic sections of the large right colon mass demonstrated a densely cellular tumor composed of pleomorphic, poorly defined, fusiform and spindle-shaped cells, the cytoplasm having indistinct borders and demonstrating a fibrillar structure in some areas. In many areas they resembled smooth muscle cells. The chromatin network of the nuclei was coarse and clumped. In some areas the nuclei were plump and oval, in other areas elongated and spindle-shaped. In general

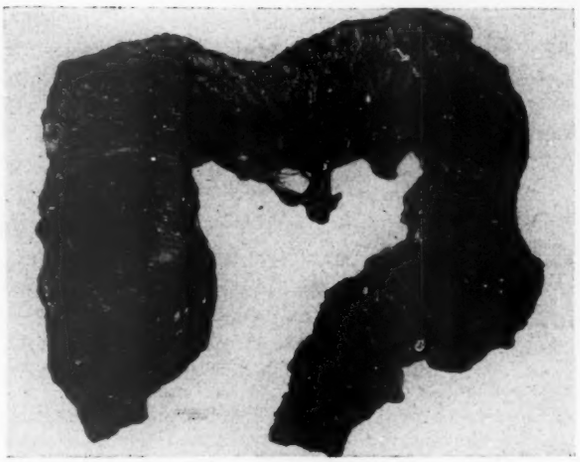

FIG. 3. Opened gross specimen showing large lesions in ascending colon, splenic flexure and sigmoid colon.

FIG. 4. Portion of sigmoid colon showing multiple small sessile polyps.

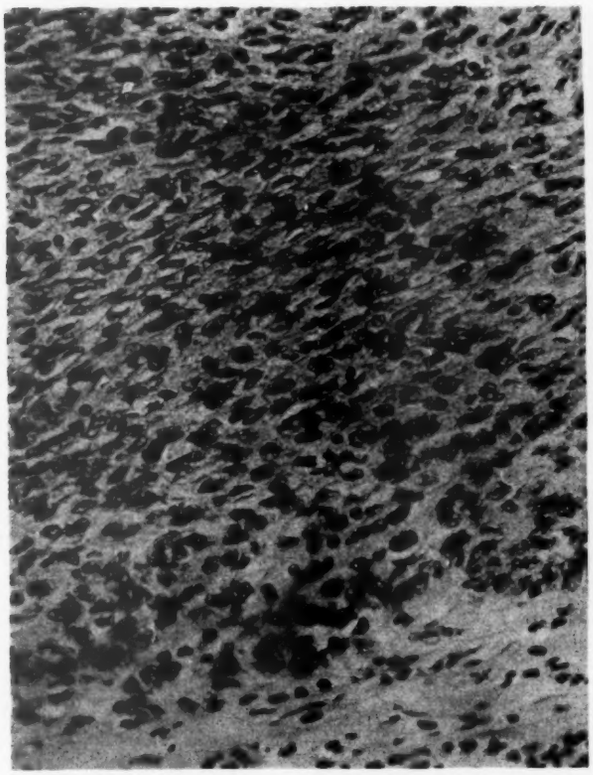

FIG. 5. Microscopic appearance of leiomyosarcoma of ascending colon. Original magnification, × 320.

FIG. 6. Section of portion of large adenomatous polyp in sigmoid colon. Original magnification, × 12.5.

the nuclei were quite large and an occasional giant nucleated cell was seen. Mitotic activity was infrequent.

The cells were arranged in interlacing bundles and whorls. The tumor had no definite capsule, was situated submucosally for the most part and was invading the lamina propria and the mucosa, causing distortion and flattening of the epithelium, and ulceration in many areas. The epithelial cells themselves appeared normal. On its deep aspect, the tumor was invading and disorganizing the smooth muscle coats of the bowel wall. (Fig. 5.) The subserosal nodule was of the same histologic pattern and appeared to be invading its fibrous capsule. Histologically, the nodule had no connection with the main tumor and presumably represented an intramural metastasis. Special staining technics (Van Gieson) indicated that the tumor was

not of fibrous tissue origin. The diagnosis was leiomyosarcoma.

Sections of the two large polypoid tumors showed them to be broad-based adenomatous polyps. The one from the splenic flexure had a very delicate papillary network of well differentiated mucous cells, and the bases of the glands had an unusual number of Paneth cells. The lesion in the sigmoid showed a moderate degree of cellular hyperchromatism and atypism. There was no invasion in either of these tumors and they were both benign adenomatous polyps.

Sections of several of the small innumerable mucosal protuberances demonstrated them to be adenomatous polyps showing varying degrees of cellular atypism and hyperchromatism, but there was no evidence of frank malignancy in any of them. (Fig. 6.) The fifty-five lymph nodes removed from the specimen showed no evidence of metastases.

The patient was readmitted to the hospital on September 9, 1956, at which time he had gained weight and was having three to four semiformed stools per day. Proctoscopy showed some evidence of edema and inflammation at the level of the anastomosis. Inspection of the remaining rectum revealed an amazing increase in the number of the small, sessile polyps, numbering approximately three dozen and ranging in size from 2 to 4 mm. in diameter. The largest of these were biopsied, and the remainder were fulgurated.

The biopsied specimens were interpreted as adenomatous polyps showing cellular atypism. The patient was again discharged from the hospital to be followed up by the surgical service at monthly intervals for proctoscopy and fulguration, as indicated by the findings. In view of the cellular atypism of the polyps removed, resection of the remaining rectum is being seriously considered.

SUMMARY

An interesting case of leiomyosarcoma of the ascending colon coexistent with multiple polyposis is presented. We believe this to be the first reported case of this condition.

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Basal Cell Carcinoma of the Perianal Region

IRVING ROSENBERG, M.D., *Philadelphia, Pennsylvania,* AND SOL ROSEN, M.D., *Millville, New Jersey*

BASAL cell carcinoma of the anorectum is a very infrequent condition. So few cases have been reported that recognition, treatment and prognosis are poorly defined. A condensation of previously reported cases is presented and one new case added. (Table I.)

CASE REPORT

R. H., a forty-nine year old white woman, was admitted to the Rolling Hill Hospital, Elkins Park, Pennsylvania, on May 1, 1957 with the chief complaint of rectal pain of two weeks' duration. Anal prolapse on defecation had been noted for the past year but was not marked or symptomatic in any other way.

The past history was interesting in that carcinoma of the uterus had been treated nine years before by hysterectomy.

Positive physical findings were confined to the anorectal area. Internal prolapsing hemorrhoids

TABLE I

Author	Age (yr.) and Sex	Clinical Description	Treatment	Result
Buie and Brust, 1933	53,F	Advanced, annular	Colostomy with posterior resection	Recurrenct, 9 mo.; died
Buie and Brust, 1933	53,F	Orange-sized lesion with inguinal mass	Refused	Unknown
Guess, 1935	52,M	2 cm., circumscribed	Local excision and radon seeds	No recurrence; died of coronary occlusion 5 mo.
Keyes, 1937	52,F	Local mass	Excision and x-ray	Died of recurrence
Tucker and Hellwig, 1938	43,M	2 cm., circumscribed	Local excision and radium	No recurrence 3 yr. postoperatively
Lawrence, 1941	73,M	Annular, invading prostate and urethra	Palliative colostomy and posterior resection	Recurrence, 2 yr.; died
Lawrence, 1941	73,M	Annular, invading perirectal spaces	Colostomy and posterior resection	Died postoperatively, no autopsy
Gabriel, 1946	70,M	1 to 2 cm., circumscribed	Local excision	No recurrence at 1 yr.
Gross, 1948	49,M	2 cm. ulcer anterior to anus	Local excision	No recurrence after 2 yr.
Lott and Alexander, 1949	62,F	Induration of mucosa 1 by 1 cm.	Excision and 5,500 r	No recurrence, 6 mo.
Bacon, 1949	60,M	Local mass	Abdominoperineal resection	Recurrence, 19 mo.; died
Bacon, 1949	52,F	Local mass	Resection and node dissection	Died, 9 mo.
Gross, 1951	71,M	Anal lesion	Local excision	No recurrence after 2 yr.
Hall, 1952	58,M	Polypoid, 1.5 cm.	Excision	No recurrence to date
Klippel and Tomlinson, 1954	65,M	Nodule 1 cm. in fistulous tract	Radiation and abdominoperineal resection	X-ray failed and resection was then performed
Manheim and Alexander, 1955	72,M	Perianal bluish swelling size of nickel with fistulous opening	Local excision	No recurrence, 4 yr.
Case and Caldwell, 1956	72,F	2 cm. circumscribed	Radiation and colostomy	Died 6 mo. after radiotherapy
Rosenberg and Rosen, 1957	49,F	1 by ½ cm. perianal ulcer	Local excision	Too early to evaluate

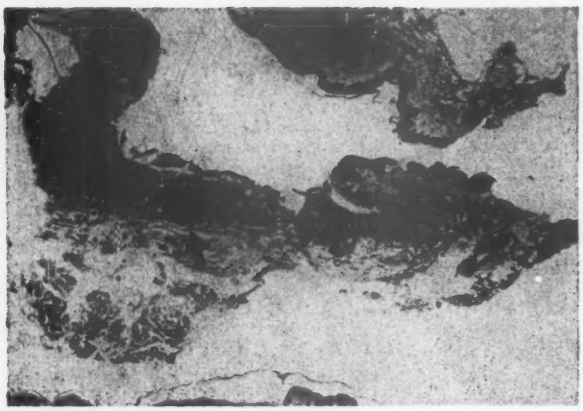

FIG. 1.

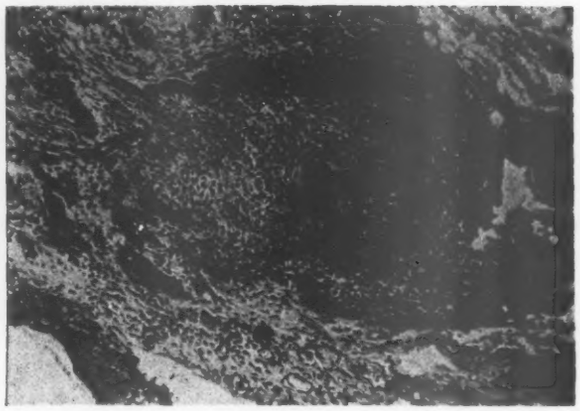

FIG. 2.

were noted with a resolving thrombus in the left lateral external hemorrhoid. The right anterior perianal skin was the site of a shallow ulcer approximately 1 by ½ cm in diameter. There was no marked discoloration and the edges of the ulcer were heaped up. Although the diagnosis was not made at that time, the lesion resembled a rodent ulcer, commonly seen on the bridge of the nose. Sigmoidoscopy was performed and was negative for 10 inches.

On May 2, 1957, under caudal anesthesia, the hemorrhoids were removed and the perianal skin lesion excised by wide and deep dissection.

The pathologist's report was as follows. (Figs 1 and 2.) On gross examination the specimen consists of an oval of skin measuring 1.6 by 1.5 cm. Eccentrically placed is a depressed ulcer measuring 0.8 by 0.4 cm. The ulcer extends for a distance of several millimeters into the subjacent tissue. A small circular tan discoloration of the outer surface of the skin adjacent to the ulcer measures 1 mm. in diameter and the cut surface reveals the discoloration to be restricted to the epidermis. A small piece of wrinkled rectal tissue is also present. This measures 1 cm. in its largest diameter.

On microscopic examination the specimen consists of sections of tissue in which the surface epidermis has been completely eroded. Beneath this, there is a severe chronic inflammatory reaction which surrounds small cords and nodular areas composed of tumor cells. The tumor nodules are arranged in plaques of tissue lined by a columnar type cell which encloses a more loosely arranged cluster of cells in which a slight degree of celiular polarity is maintained. The number of mitotic figures is extremely small. Intercellular bridges are not found within the tumor deposits. The lesion sends finger-like extensions into the subjacent tissues but the tumor seems to be restricted to the dermis and in these sections does not extend into the subjacent muscle. The diagnosis was basal cell carcinoma.

It was believed that a cure has been affected by the removal of the tissue but local x-ray therapy is also contemplated.

Four weeks later, the anus was perfectly healed with no evidence of hemorrhoidal tissue or ulceration.

SUMMARY

1. A case of basal cell carcinoma of the anus is reported.

2. All suspicious tissue should be subjected to microscopic examination.

3. If biopsy is generous it may be curative.

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Cholecystitis in a Four Year Old Child

FRANK E. BARNES, JR., M.D., *Smithfield, North Carolina*

GALLBLADDER disease is rare in children; only 500 cases have been reported since 1722. Ulin [1] critically reviewed the literature in 1952 and, discarding questionable cases, found that fewer than 400 cases of proved primary gallbladder disease in children had been reported up to 1948.

This is not an attempt to review the literature, since Ulin and Glenn have done so recently [1,3], but to report a case of primary gallbladder disease in a young boy.

Glenn believed that the seven cases he reported from the Pediatric and Surgical Pavilion of the New York Hospital were associated with acute systemic diseases [3]. In only one of these patients was cholelithiasis found. Gross [2] also believed that gallbladder disease in children was infectious and frequently could be treated as an infection with conservative therapy. In his text, *Surgery of Infancy and Childhood* [2], Gross reported on six patients with cholelithiasis, 50 per cent of whom had hemolytic anemia as a causative factor. Gallstones in children, which are always pigmented, should lead one to suspect a blood disorder and to investigate the spleen and blood picture thoroughly.

A great majority of these patients have been misdiagnosed. At least 15 per cent were diagnosed as having appendicitis, and many other diagnoses were believed to be intestinal obstruction. The delay in diagnosis has been stressed by the authors; the average time between onset of the first symptoms and the final diagnosis was about four and a half years.

Although gallbladder disease is unusual in youths, it is important to be aware of its existence. Many cases of gallbladder disease in children may be misdiagnosed by overlooking the persistent symptoms of nausea, vomiting, abdominal pain, diarrhea, and occasional jaundice, recurring periodically over a number of years. Consideration of this diagnosis in children does not receive the attention it merits.

The collective experience indicates that once the diagnosis is eatablished, cholecystectomy is indicated. Cholecystectomy will tide the patient over an acute episode and possibly for years to follow, but invariably he returns with recurrent gallbladder disease.

CASE REPORT

The first Nassau Hospital admission of R. R., a four year old boy, was on December 25, 1952. The chief complaint was abdominal pain of two days' duration. One week before admission, the child complained of abdominal pain, which was thought to be gastroenteritis. The symptoms subsided on conservative therapy. Two days before admission he complained of crampy pains in the umbilical region, associated with constipation. He then had no nausea or vomiting.

Physical examination revealed no abnormalities except for a slightly distended abdomen, which was tender in the right upper quadrant. A palpable mass was noted above and to the right of the umbilicus. It did not move with respirations.

Examination of the blood revealed a normal hemoglobin and a white blood cell count of 7,800 per cu. mm. with a normal differential. The urine was negative for sugar and albumin but gave a 2-plus acetone. No bile was found in the urine.

With the preoperative diagnosis of intussusception, laporatomy was performed on December 26, 1952. Exploration revealed a normal appendix, which was removed prophylactically. The mass felt preoperatively in the right upper quadrant of the abdomen proved to be a large, dense, distended, inflamed gallbladder. It was aspirated. The bile was cloudy but contained no stones. A small mushroom catheter was inserted in the fundus and brought out through a stab wound.

The child's postoperative course was satisfactory. On the seventh day after the operation, cholangiogram was performed. The gallbladder was visualized, as was the cystic, hepatic and common ducts. Dye entered the duodenum with-

out delay. No evidence of retained calculi was found.

Sixteen months later, on April 6, 1954, the boy complained of epigastric pain, had several bouts of vomiting and had to be admitted to the hospital three days later because of the persistent pain.

Physical examination again revealed no abnormalities except for the abdomen. There was considerable tenderness in the right upper quadrant, and a palpable mass the size of a golf ball was noted under the right costal margin.

Roentgen study showed normal kidney outline on both sides; there was no enlargement of the liver or spleen. There was some faint mottling in the right upper quadrant, the significance of which was not then apparent.

The laboratory examination showed an elevated white blood cell count of 11,100 per cu. mm. with a differential of 79 per cent polymorphonuclears and 21 per cent lymphocytes. Hemoglobin was 10.5 gm., with a 3.6 million red blood cell count. Urinalysis was negative.

Surgeons consulted on the day of admission believed that the patient was not acutely ill and could be observed for another twenty-four to forty-eight hours. They did think this was a recurrence of acute cholecystitis.

The day after admission, the child's temperature and pulse began to rise. A repeat blood count, taken on April 12, 1954, showed a rise in the white blood cell count to 16,600 per cu. mm. with 83 per cent polymorphonuclears and 17 per cent lymphocytes.

That evening the patient's abdomen was opened through a right subcostal incision. The gallbladder was tense and dark red. It was thick-walled and obviously inflamed. A few adhesions were attached to the gallbladder as a result of the previous operation. The gallbladder was removed in the usual manner without difficulty. The common duct was not explored, but it was felt to be free of calculi on palpation even though several small calculi were found in the fundus. The postoperative course was uneventful.

CONCLUSIONS

Gross has stressed hemolytic anemia as a cause of calculi; but other investigators have not reported it as a consistent finding. Davis, in his experience at Post Graduate Hospital, recalls two cases of gallbladder disease in children, both of whom had pigmented stones and neither of whom had a blood disorder. The few patients whom I have been able to inquire about in the New York area have had calculi, but none has had hemolytic anemia. The feeling of some authors that cholecystitis in children is part of an acute systemic disease and can be treated conservatively had been proved wrong. A diseased gallbladder should be removed.

SUMMARY

1. Incidence of gallbladder disease in children is briefly reviewed.

2. Pitfalls in preoperative diagnosis are presented, the average delay being four and a half years.

3. Hemolytic anemia as a cause of cholelithiasis is not a consistent finding.

4. A diseased gallbladder should be removed; conservative therapy is wrong.

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Sacrococcygeal Teratoma

GILMAN DEERING KIRK, M.D., *Columbus, Ohio*

SACROCOCCYGEAL teratoma is a tumor of the embryo which may present at birth in either a posterior sacral position or an anterior sacral position.

Calbet [*1*] established many years ago that sacral tumors of all types occur in about one case per 35,000 births. This fact has been reconfirmed several times, including Whitaker and Pemberton's [*2*] report from the Mayo Clinic in 1938.

Pathologically there is a high rise in malignant potential the longer the tumor remains *in situ*. Hickey and Layton [*3*] showed a 95 per cent benign character up to four months after birth with a rise to 65 per cent malignancy by the age of two years.

Embryologically there has been much speculation as to the origin of the sacral tumor but the generally accepted theory today is well explained by Gross [*4*] in which he discusses the concentration of primitive cells at Hensen's node located near the coccyx. These cells are considered to be totipotent or capable of producing cells of any of the three germ layers. Hence, they may produce a teratoma at the site. The other totipotent site is the reproductive anlage. Hence, the frequency of teratoma of the ovary is found.

It is also significant that the large majority of patients are females, as were our two patients presented herein. There does not seem to be any adequate explanation for this fact.

Willis [*5*] carefully discusses the differential diagnosis from caudally attached twins, supernumerary limbs and, most important, meningocele.

Schiffer and Greenberg [*6*] discuss the dangers of dystocia in labor when a large teratoma is present. They also caution against radical distractive delivery during labor.

Clinical history is of no particular significance although Ravitch and Smith [*7*] point out the frequency of constipation and urinary obstruction in their excellent general review of forty-eight cases.

CASE REPORTS

CASE I. This white newborn female infant was admitted to Children's Hospital on June 25, 1954, with chief complaint of large tumor mass in the sacrococcygeal region. The patient was delivered by Cesarean section because of bleeding and cramping during the later stages of pregnancy. At delivery a large, soft mass was noted protruding from behind the rectum and the patient was sent to the hospital for definitive treatment the day of birth.

Physical examination revealed a thin newborn infant weighing about 9 pounds. About half of this weight was contained in a large mass which protruded from behind the rectum. The mass was 20 by 15 by 15 cm. It arose from the retrorectal area and distended the rectum forward. The mass was covered with small, thin-walled veins. It was soft and not apparently cystic. It was transilluminated in areas and had a solid core of tissue. The remainder of the physical examination was within normal limits. A diagnosis of sacrococcygeal teratoma was made. (Fig. 1.)

The baby was taken to the operating room the following day and while under vinethene® and ether anesthesia, with an intravenous solution running in the ankle, was prepared for surgery.

A long oval encircling incision was made and the tumor dissected off the sacrum and gluteal muscles. The tumor was not attached to the rectum nor did it invade the area anterior to the coccyx. Hemostasis was effected and the area was closed, as noted in Figure 2.

The hospital course thereafter was essentially uneventful although the patient gained weight very slowly. She was discharged at the end of three weeks as recovered.

At the end of three years the mother reports her as a normal healthy child with no evidence of trouble other than a visible scar.

CASE II. A white female baby, three days old, was admitted to Children's Hospital on June 24, 1947, because of a mass protruding from the area between the buttocks and sacrum.

FIG. 1. Case II. Newborn baby with sacrococcygeal tumor.

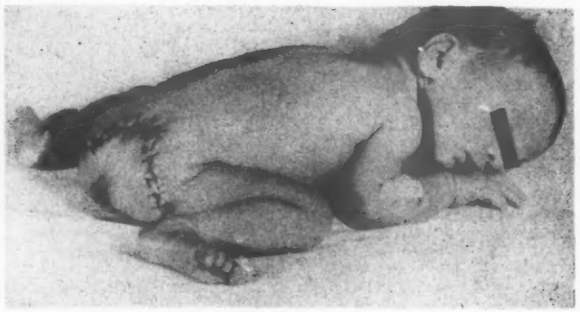

FIG. 2. Case II. Patient three days postoperatively.

Physical examination revealed an essentially normal female baby with a mass behind the rectum which on rectal examination distended the tissue between the rectum and the sacrum almost collapsing the rectum. A diagnosis of sacrococcygeal tumor was made and she was prepared for surgery.

At surgery the tumor mass was dissected out from the retrorectal tissues and was apparently encapsulated. It did not involve any nerves and was found to be partly solid and partly cystic.

The pathology report revealed benign teratoma containing cartilage, bone, intestine, skeletal muscle, fat, trachea, lymph nodes, brain and thyroid tissue. The baby made an uneventful recovery and was discharged.

One year later she was readmitted because of a large intra-abdominal tumor which was interfering with urination and bowel elimination and recently associated with vomiting and pain. A barium enema showed the sigmoid pushed far to the right by a slightly opaque mass.

The patient was prepared for surgery and through a laparotomy incision a large cystic mass was found to fill the pelvis extending down behind the sigmoid. Because of its size and position it was decided to marsupialize and pack the cyst.

Postoperatively the gauze was gradually removed, the cavity closed completely and the baby was sent home.

Five years later, after having some retrorectal drainage from a small cyst, the patient was taken to the Cleveland Clinic where surgery was not advised.

A few months later she was operated upon by another surgeon for a recurrent retrorectal mass with displacement of the sigmoid and bladder.

At surgery this third time a presacral approach was made and after four and a half hours of surgery and 1,700 cc. of whole blood transfusions the tumor was removed. The patient had a stormy postoperative course but recovered. She is now ten years old and developing normally with no further recurrence.

SUMMARY

Two further cases of sacrococcygeal tumor are reported emphasizing the classical location of presacral and postsacral position. The rare incidence, the postulated etiologic theories and the propensity to malignancy are discussed. Newborn infants tolerate the extensive surgery when careful surgical principles are followed. The anterior type of sacrococcygeal teratoma may present very formidable surgical obstacles. These babies later develop into normal children without neurologic, rectal or urologic defects. There is no satisfactory explanation for the high incidence of occurrence in female babies.

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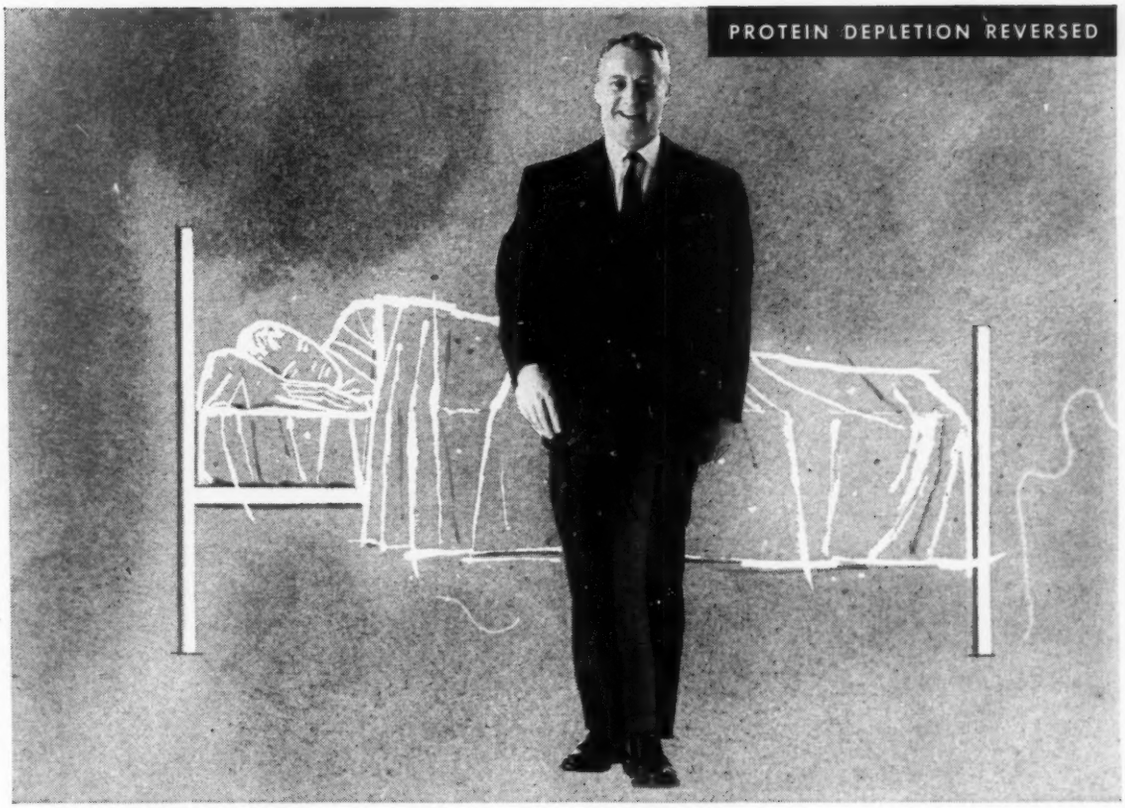

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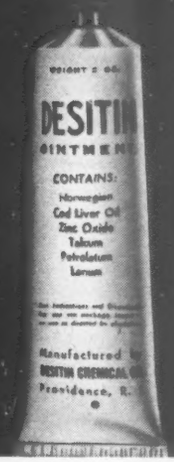

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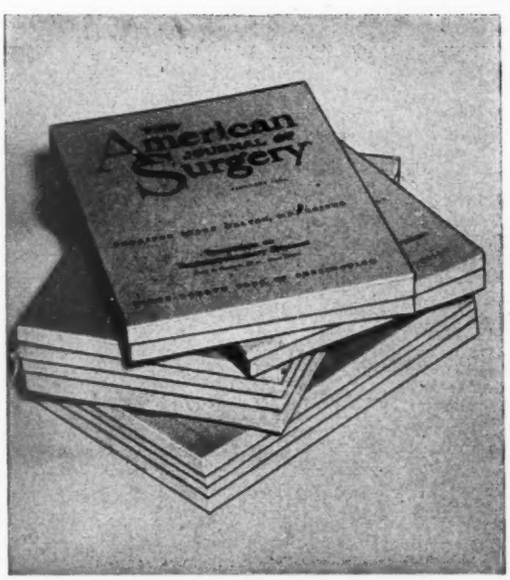

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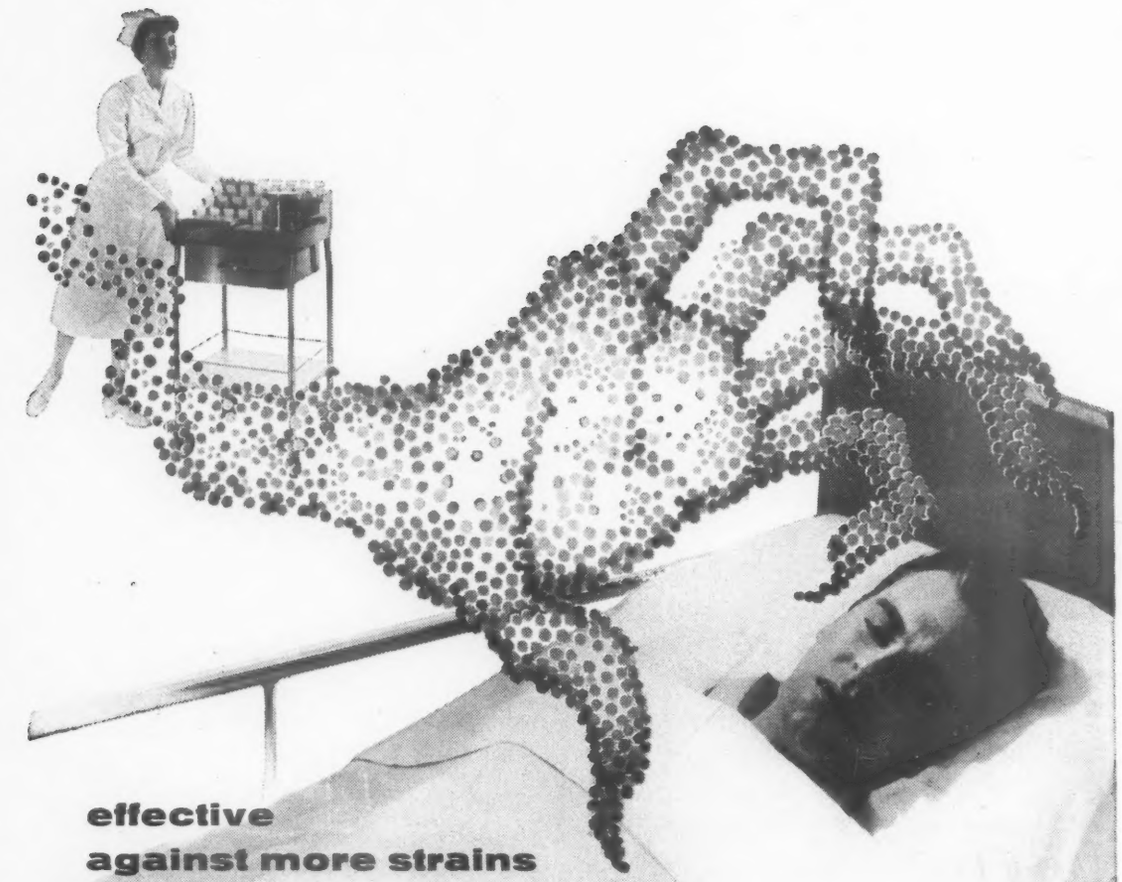

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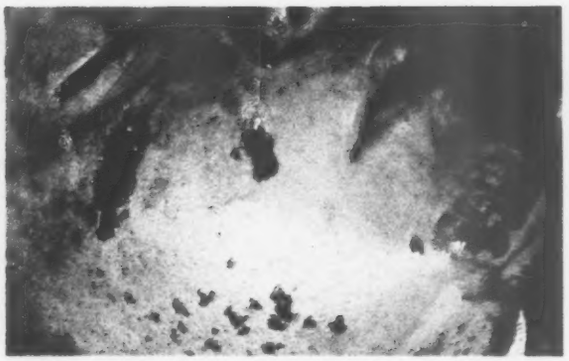

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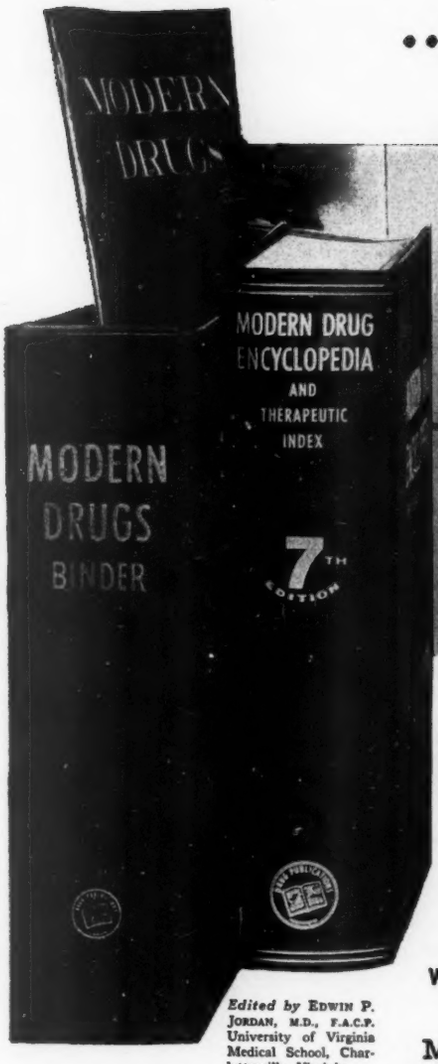

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1. Granberry, C., and Beatrous, W. P.: E.E.N.T. Mo. 36:294 (May) 1957. 2. Rittenhouse, E. A.: E.E.N.T. Mo. 36:406 (July) 1957. 3. Fox, S. L.: Clin. Med. 4:699 (June) 1957.

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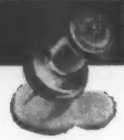

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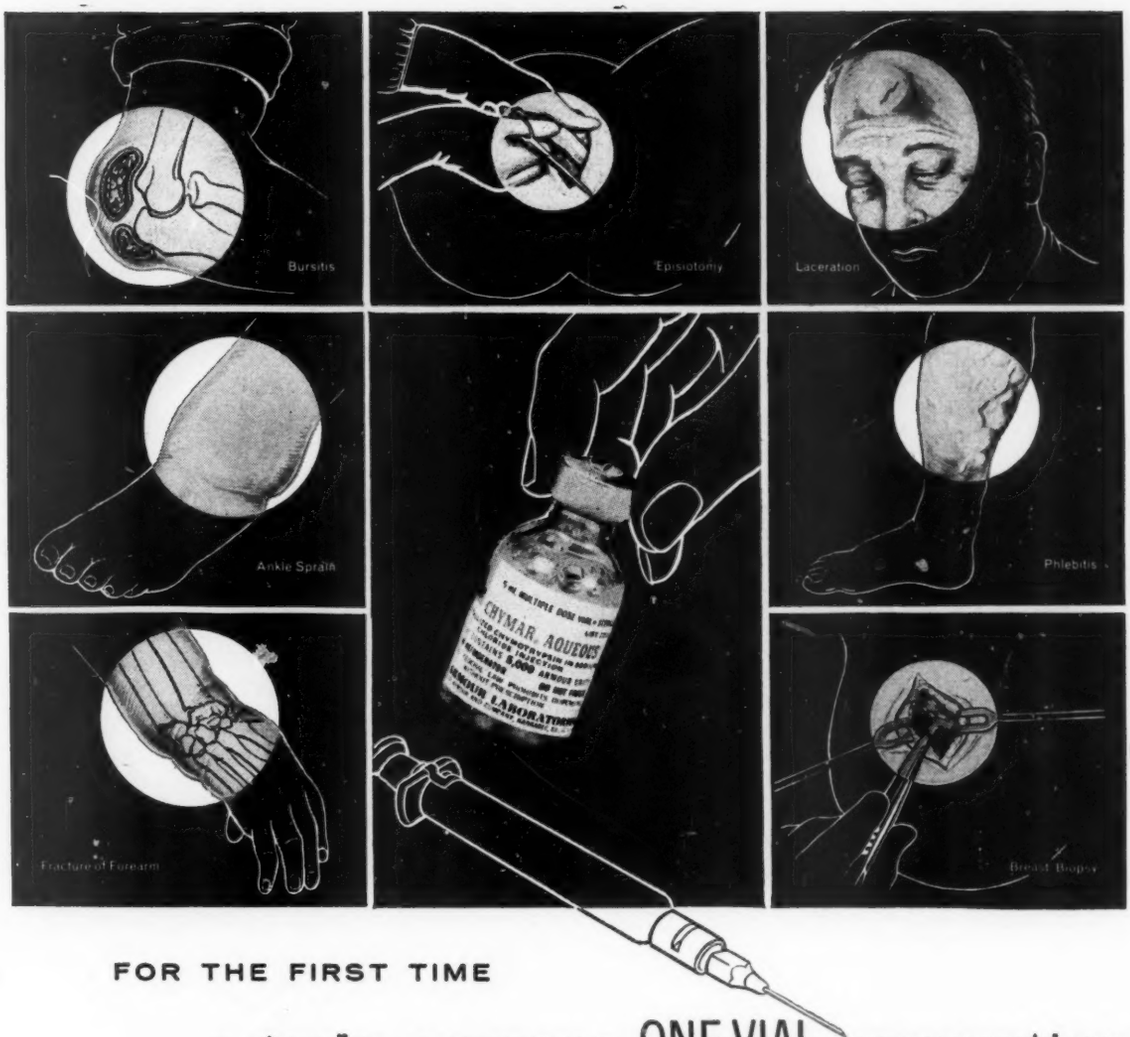

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NOTES AND QUOTES

WARNER-LAMBERT RESEARCH INSTITUTE. The establishment of a Warner-Lambert Research Institute was announced recently by Alfred E. Driscoll, President of Warner-Lambert Pharmaceutical Company.

To head the Warner-Lambert Research Institute, Mr. Driscoll has announced the appointment of Dr. L. Earle Arnow as its President, who will assume responsibility for the over-all administration of research of the various divisions of the company.

Dr. Arnow has been a Vice-President of Merck Sharp & Dohme Research Laboratories, and the Executive Director of the Merck Institute for Therapeutic Research since 1954. Prior to this, he was Vice-President for research of Sharp & Dohme.

"The establishment of the Warner-Lambert Research Institute is an important step in our program to consolidate and strengthen all of the company's major research activities," Mr. Driscoll said in making the announcement.

Headquarters of the new Warner-Lambert Research Institute will be at the company's headquarters in Morris Plains, New Jersey, where a new research laboratory building for its Warner-Chilcott Laboratories division was dedicated just a year ago.

OF INTEREST TO DIABETICS. *Seven of ten diabetic persons who contract the disease as adults may be freed from dependence on hypodermic insulin injections through prescribed daily dosages of a new drug in tablet form for oral control of the disease, according to medical findings reported in the current issue of* Monsanto Magazine.

Trademarked orinase, the drug is a German discovery manufactured in the United States by The Upjohn Company, Kalamazoo, Michigan. Chemically, it is tolbutamide, a compound produced from a complex organic chemical supplied by Monsanto Chemical Company.

Medical authorities estimate that there are two million diabetics in the United States, half of whom do not yet know that they are victims of the disease. The milder, "adult" type of diabetes afflicts an estimated 85 per cent of this total, and it is among these that orinase may offer escape from the discomforting and often dreaded needle, the article states.

Tests of the drug have been carried out since November, 1955, by 3,000 physicians and 400 clinics on thousands of diabetic patients, the article points out, and are continuing even though the Food and Drug Administration already has approved the prescription sale and use of the drug.

PRODUCTION OF CORTICAL HORMONES. Discovery of a new and unique process to speed production of cortisone and other cortical hormones has been reported by Dr. Howard J. Ringold, Director of Chemical Research for Syntex, Mexico City steroid hormone manufacturer, and Dr. Gilbert Stork, Professor of Chemistry at Columbia University and a Syntex research consultant.

In a communication addressed to the editor appearing in a recent issue of the *Journal of the American Chemical Society*, Doctors Ringold and Stork reported on a process for the introduction of a 21-hydroxyl group into compounds containing a delta 4-3-keto system (a,b-unsaturated ketones). The 21-hydroxyl group is an integral part of all the adrenocortical hormones used in the modern treatment of various disorders such as arthritis, skin allergies and certain eye disorders. The best known of this group of hormones are prednisone, prednisolone, cortisone and hydrocortisone.

This new process replaces a long and complicated procedure and will result in a more plentiful supply of these cortical hormones that are in such great demand.

Syntex is the organization which pioneered in the research and development of the "nor" compounds. These have recently received worldwide attention for their unprecedented effectiveness in treating certain female endocrine disorders such as infertility and threatened and habitual abortion, among others.

Dr. Stork was last year's winner of the American Chemical Society's Award in Pure Chemistry.

HEART DISEASE. *Heart attacks strike far more often when a person is resting than when he is working, according to a recent issue of the new monthly publication,* Patterns of Disease.

Published by Parke Davis & Company, this publication is designed to provide the latest available statistical information on major U. S.

CONTINUED ON PAGE 52

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August 1958

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health problems such as old age, arthritis, allergic diseases, diabetes and mental health. A recent issue focuses on cardiovascular disease which now claims one of every two American lives.

Approximately 30 per cent of all coronary heart attacks occur when people are resting, and a mere 2 per cent when they are engaged in "sports, running, lifting or moving a load," according to Patterns.

"Several studies indicate that the highest death rate in males occurs among those employed at sedentary jobs," it says.

Moreover very few cardiac patients need to curtail their activities drastically. "The majority of persons disabled by heart disease recover from attacks to live many years and most are able to resume work," Patterns *states. Less than 1 per cent of all victims of heart disease require complete rest.*

What are some of the factors which contribute to the death rate in heart disease? Patterns *discloses that these include such diverse elements as the weather, sex, geographical location and the type of heart disease.*

For instance, studies show that deaths from heart disease tend to rise during the winter months and to decline during the summer. They further reveal that heart disease takes a far greater toll among men than women—a difference which has been steadily mounting over the past few decades. Thus within the last forty years the heart disease death risk within the forty-five to sixty-five year age group has increased nearly 25 per cent for men and decreased at almost the same rate for women.

Death rates for heart disease vary too from state to state, with the New England states heading the list and southwestern states such as Arizona and New Mexico ranking last.

As far as classification is concerned, Patterns *cites hypertension and arteriosclerosis as accounting for over 90 per cent of deaths for cardiovascular disease, including vascular lesions affecting the central nervous system and myocardium. Coronary heart disease remains the leading heart problem.*

However the publication adds that "With adequate care, 22 per cent of patients with heart disease can expect improvement or halting of progress of the disease, compared with only two per cent improvement for those without care."

The need for adequate treatment is underscored by the fact that deaths from cardiovascular disease are rising rapidly. According to Patterns, *the proportion of deaths due to cardiovascular disease has increased from about 20 per cent in 1900 to almost 55 per cent in 1956.*

Moreover costs for the disease have been increasing dramatically. They now amount to more than $3 billion worth of working time in the United States, and a loss in income tax to the Federal Government of almost $4 million.

BENEFIT HEALTH INSURANCE PAYMENTS. Benefit payments by insurance companies to Americans protected by health insurance policies amounted to a record $2.5 billion in 1957, the Health Insurance Institute recently reported. This figure, the Institute said, represents a 16.1 per cent increase in benefit payments over the $2.1 billion paid in 1956.

Latest figures supplied by the U. S. Department of Labor in its 1957 Consumer Price Index showed that medical care costs during the year rose by 4 per cent.

The Institute report is based upon a survey of the nation's insurance companies writing policies which help pay for doctor and hospital bills and for loss of income incurred as a result of accident or sickness.

The survey revealed that reimbursements through group insurance plans in force during the year totaled $1.8 billion, or 21.3 per cent over 1956, while payments through individual and family type policies amounted to $619 million, a rise of 3 per cent over the previous year.

Payments to policyholders covered under hospital expense insurance policies, the Institute further reported in listing the figures by type of service, amounted to over $1 billion, with $778 million paid under group policies and $224 million paid by insurance companies to individual policyholders.

Reimbursements to defray the cost of surgeons' fees totaled $398 million, with $322 million received by holders of policies under group plans, and $76 million paid to persons covered by individual surgical expense insurance policies.

Persons covered for non-surgical medical care and treatment through regular medical expense

CONTINUED ON PAGE 54

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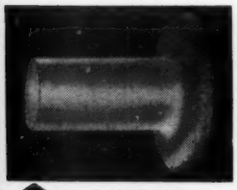

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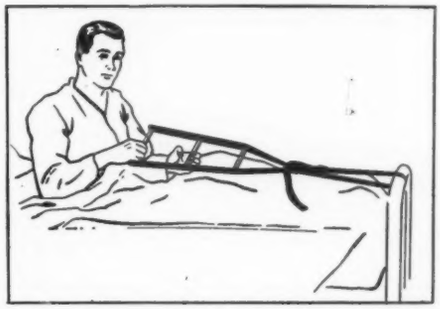

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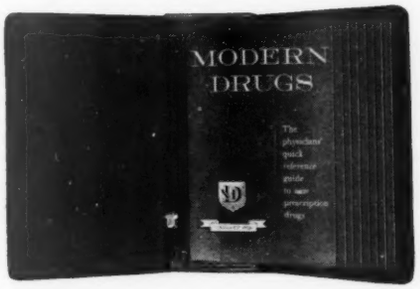

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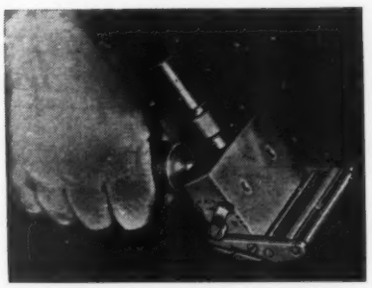

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insurance policies received a total of $71 million during the year. Group policyholders received $61 million while those covered by individual policies were paid $10 million.

Benefit payments to those protected against the cost of serious, or catastrophic illness or accident through major medical expense insurance policies, including supplemental and non-supplemental coverage to the basic health cost plans, amounted to $130 million. Group plan payments totaled $126 million, while individual contract benefits came to $4 million. Of particular note, added the Institute, is the fact that payments in 1957 through major medical policies, the fastest-growing form of health insurance, increased by 100 per cent over the year 1956.

In concluding its report of payments for health care by the insurance companies throughout the United States, the Institute stated that the increase in such payments reflects the continued efforts of the public to pay its doctor and hospital bills through the voluntary non-governmental mechanism.

The Health Insurance Institute is the central source of information for the nation's insurance companies serving the public through voluntary health insurance.

ELECTRIC "HOTFOOT." *A new laboratory test for tranquilizing agents that uses an electric "botfoot" to make mice fighting mad at each other has been described by three scientists from Smith Kline & French Laboratories.*

A pair of normally peaceful mice are placed on an electrically charged grid, with a large glass beaker serving as a kind of boxing ring. Then the "botfoot" is administered—five per second.

At the outset, the Smith Kline & French group reported, the mice jump around to avoid the shocks. However, after a brief period the mice "converge at close quarters, stand face-to-face on their hind legs, and spar and bite savagely at one another." To the casual observer it looks as though each mouse decided the other was responsible and decided to hit back.

When the animals are given various tranquilizing agents and other drugs that depress central nervous system activity, they jump when shocked, but do not fight.

The "mouse rage" test has become part of the battery of animal behavior tests used by Smith Kline & French to obtain a pharmacological profile of a drug before the compound is tried in humans. The test also is valuable in screening compounds for specific activity.

SKIN TYPING. Skin typing in fashion similar to that of blood groups may be possible some day if scientists can find a way to eliminate a defense mechanism of the body which causes eventual rejection of transplants in nearly all cases except those between twins. The possibility was raised at the Symposium on Genetics in Medical Research at the University of Wisconsin Medical Center.

Dr. Ray Owen, former University of Wisconsin faculty member, now Professor of biology at California Institute of Technology, discussed skin typing following the presentation of a paper on "Transplantation and Acquired Tolerance."

The major deterrent is a defense mechanism which causes a delayed reaction of incompatibility and eventual rejection of attempts at permanent transplantation. Identification and subsequent elimination or nullification of the defense mechanism would advance the study toward eventual skin typing, he indicated.

"Then," said Dr. Owen, "If we had a tool for typing skin in fashion similar to blood typing, it might prove extremely helpful, particularly in situations where large amounts of skin from volunteer donors are needed following major disasters."

Cases are on record, the geneticist pointed out, in which very ill patients in the final stages of disease have received grafts or transplants from non-identical genetic sources which were not rejected.

TOUR TO ISRAEL. *The American Physicians Fellowship, Inc. for the Israel Medical Association is sponsoring an all-inclusive tour to Israel for the 4th World Medical Assembly of the Israel Medical Association, to be held in Tel Aviv, Haifa, Jerusalem, August 12–24, 1958. The tour group will depart from New York via El Al Israel Airlines on August 9th, and will leave Israel on August 24th. For further details, contact the National office at 1330 Beacon Street, Brookline 46, Mass.*

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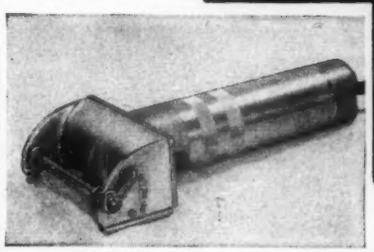

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*Koch, R., and Donnell, G.: California Med. 87:313, 1957.

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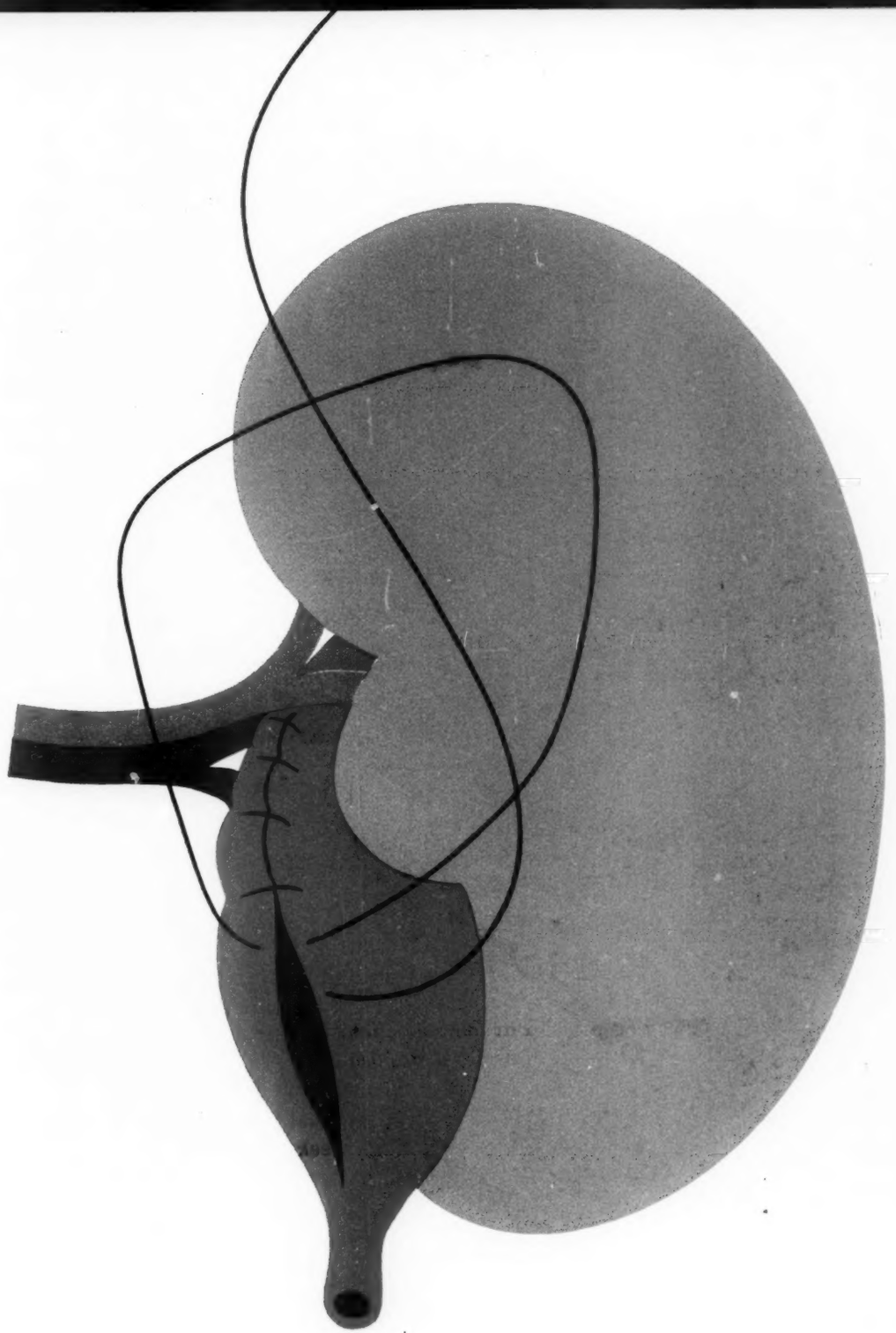

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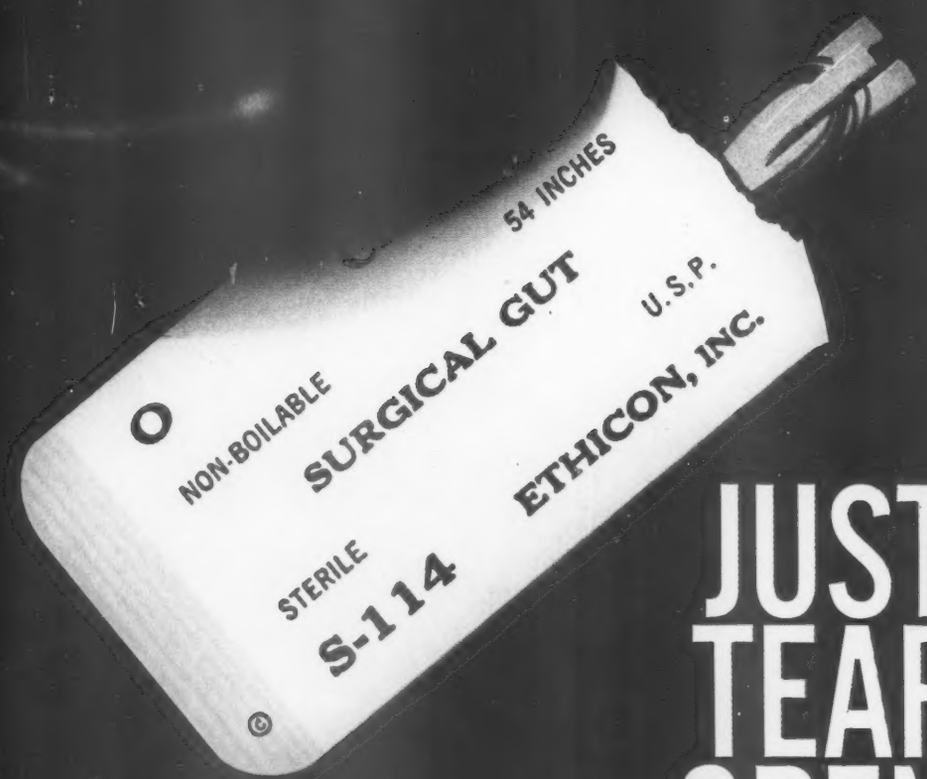

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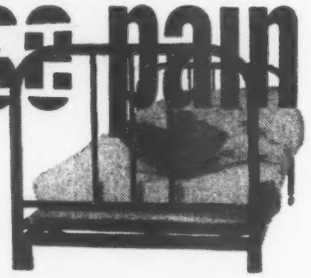

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1. Keesling, R., Hinds, E. C., and Keats, A. S.: Principles of Drug Evaluations in Dental Surgery: Antihistamines and Analgesics: (Paper read at the Thirty-fifth Gen. Meeting of the International Assoc. for Dental Research: Atlantic City, March 21-24, 1957). 2. Orahovats, P. D., Lehman, E. G., Chapin, E. W.: Pharmacology of Ethyl-1-(4-Aminophenethyl)-4-Phenylisonipecotate, Anileridine, A New Potent Synthetic Analgesic: Journal of Pharmacology and Experimental Therapeutics, Vol. 119, No. 1, (January) 1957. 3. Stage, J. T.: Anileridine as an Anesthetic Agent: Journal of the Florida Medical Association 44:143-145 (August) 1957. 4. Keats, A. S., Telford, J., Kurosu, Y.: Studies of Analgesic Drugs: Anileridine Dihydrochloride: Anesthesiology 18:690-697 (September-October) 1957 . 5. Riffin, I. M., Preisig, R., Wheaton, H. H., Landman, M. E., and Schwarz, B. E.: "A New Synthetic Analgesic, Anileridine," Scientific Exhibit, 106th A.M.A. Annual Meeting, New York; June 3-7, 1957.

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